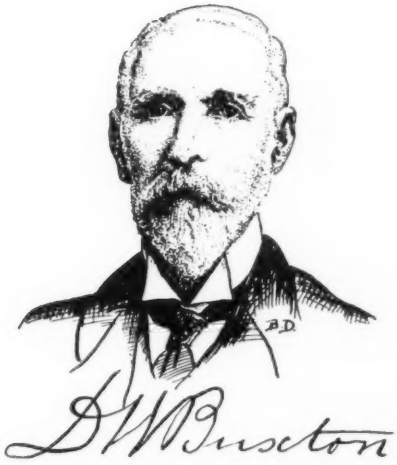

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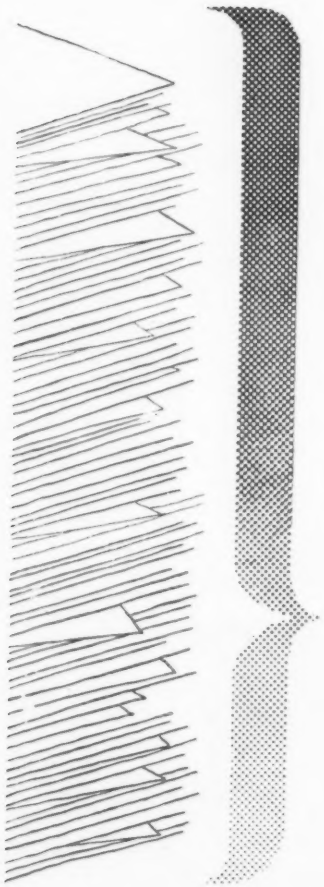

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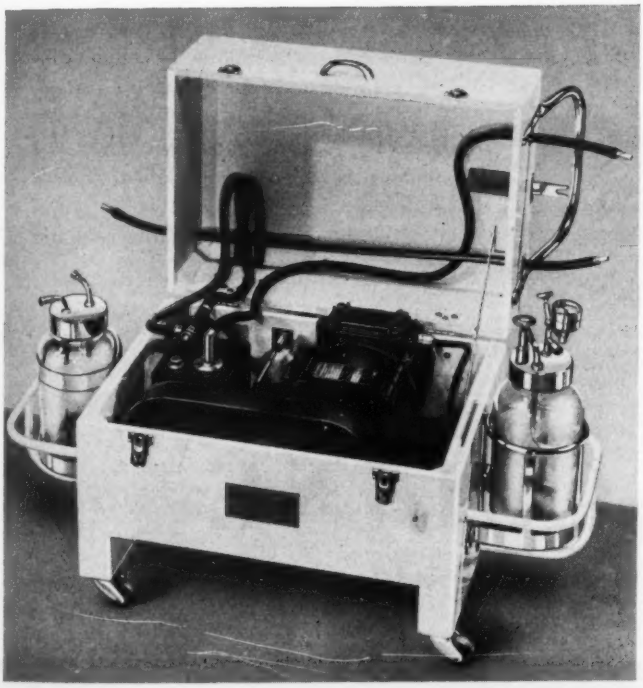

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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXIX No. 5 MAY 1957

EDITORIAL

FIRST THINGS FIRST

"Science is a first-rate piece of furniture for a man's upper chamber if he has common sense on the ground floor. But if a man hasn't got plenty of good common sense, the more science he has the worse for his patient."

Holmes: *The Poet at the Breakfast-Table.*

Only twenty years ago it was widely considered strange that a practitioner of active mind and reasonable academic achievement should decide to devote his life to the specialty of anaesthesia. It was considered that it offered too limited a horizon for such an individual and that the mastery of the techniques then available would soon result in boredom and frustration. The anaesthetist's duty was to administer the anaesthetic and little else was expected. But new methods and techniques were absorbing the attention and interest of anaesthetists and they revealed an unexpected skill in venepuncture, in laryngoscopy and endotracheal intubation, in the use of tracheobronchial suction, and inevitably thereafter in bronchoscopy. The confident handling of the curarized, apnoeic patient led to the realization that here was the practitioner best qualified and equipped to deal with patients suffering from respiratory paralysis—and if the patient had tetanus, a relatively intractable condition, let him be turned into a case of respiratory paralysis which the anaesthetist knew how to treat. Such conditions, especially when mechanical respirators appeared, encouraged a wider and more precise knowledge of respiratory physiology and of biochemistry and their terms became part of the daily jargon of anaesthesia.

Absorption of the anaesthetist into the surgical team has been accomplished and he tends to become the physician, physiologist and indeed the pharmacologist of his group. That he has still much to learn was made clear by speakers at the recent Symposium on Anaesthetic Teaching held at the Postgraduate Medical School. But at least the recruit to anaesthesia has nothing to fear for his future interest. He, or increasingly and acceptably she, is entering a specialty rich in opportunity, with an unlimited scope for interesting observation, investigation and research. But he must remember at all times that his first duty as a member of the surgical team is to the patient. To most anaesthetists, service to the clinical needs of the patient and the surgical work of the hospital must be a first charge.

This charge, however, should not be impeded, as is the present tendency, by the too ready acceptance of responsibility for everything except the actual surgical procedure. That the anaesthetist is finding his hands overfull is suggested by the readiness with which he allows even untrained personnel to prepare for him the various intravenous drugs which he expects to use, as well as intravenous infusions of varying kinds not excluding blood. In such circumstances there can be little doubt upon whose shoulders the responsibility would lie if a wrong injection is made.

Thus, though anaesthetists must be gratified by the oblique compliment paid to them in their increasing responsibilities, they must be equally on their guard to preserve their true functions during the operation phase of the patient's treatment, namely, to anaesthetize the patient as safely and as simply as is compatible with the needs of the case, and to beware of the increasing responsibilities which might divert them from this purpose.

Brit. J. Anaesth. (1957), **29**, 194

COMPARISON OF SEVEN INTRAVENOUS ANAESTHETIC AGENTS IN MAN*

BY

GORDON M. WYANT, ALLEN B. DOBKIN AND GEORDIS M. AASHEIM

FROM time to time new agents used in anaesthesia are synthesized with a view to improving upon or superseding established drugs. This is a welcome trend, since once in a while an agent is found which is, in many respects, superior to previously known drugs and which fills a definite clinical need. Most of the new agents, however, must be discarded, not so much because of their lack of clinical suitability but because the clinician finds no real need for the new drug. Frequently the promising impressions gained from animal experiments are not fufilled when the agent is subsequently tested in man. When it does come up to expectations, the clinician must still determine whether the new drug has sufficient advantages over established agents to warrant its introduction into clinical anaesthesia, however good the new drug may be. If critical comparisons are not carried out, the market becomes saturated with innumerable similar compounds all claiming this or that advantage over the other, but none serving a really useful purpose. Clinical impressions of new agents are notoriously misleading. After the pharmacological properties of the agent have been established in animals, it becomes the duty of the clinician first to determine, as far as possible, the pharmacological properties of the new drug in man and, if possible, to compare them quantitatively and qualitatively with those of established agents which serve as standards for comparison. If such comparative studies under controlled conditions suggest to the investigators that there is some merit in a new drug, then and only then, should it be used under actual clinical conditions in order to assess its usefulness when administered after pre-operative medication, with other anaesthetic agents, and in the presence of the many complicating factors due to disease and operation.

In the past, anaesthetists, as a group, have been much too indulgent in accepting new agents which, although they have enjoyed a brief period of popularity, have soon fallen into disuse or have found very limited application in only a few centres. If these drugs had never reached the open market, anaesthesia would have been none the poorer.

With these thoughts in mind we have compared under controlled conditions the comparative properties of seven intravenous anaesthetic agents in man. Three of these agents are clinically established barbiturates; three others are new or experimental barbiturates; and one is a new non-barbiturate drug. We have attempted to determine whether any of the four new agents have sufficient merit to recommend their adoption for clinical use, and we have also attempted to re-evaluate some of the properties in man of the three established drugs.

The seven drugs studied, their generic names, chemical names and structural formulae are listed in table I. With the exception of Dolitrone, they are all barbiturates. All agents are sodium salts of an acid and are dispensed in powder form. They are dissolved in distilled water or normal saline prior to use because the solutions tend to deteriorate after varying periods of time. Dolitrone deteriorates quite rapidly in solution and must be prepared immediately prior to use. Pentothal (thiopentone), Surital (thiamylal) and Transithal (buthalitone) are yellowish powders; Evipal (hexobarbitone), Neraval (methitural), Compound 25398 and Dolitrone are white.

The pH of solutions of the seven agents,

* From the Department of Anaesthesia, University of Saskatchewan College of Medicine and University Hospital, Saskatoon, Canada.

TABLE I

Formulae

Trade name	Official name	Chemical name
PENTOTHAL (Abbott)	Na Thiopentone	Na 5-Ethyl-5-(1-Methylbutyl)-2-Thiobarbiturate
SURITAL (Parke-Davis)	Na Thiamylal	Na 5-Allyl-5-(1-Methylbutyl)-2-Thiobarbiturate
EVIPAL (Winthrop-Stearns)	Na Hexobarbitone	Na N-Methyl-5-Cyclohexenyl-5-Methyl Barbiturate
TRANSITHAL (Poulenc)	Na Buthalitone	Na 5-Allyl-5-Isobutyl Thiobarbiturate
NEMAVAL (Schering)	Na Methitural	Na 5-(1-Methylbutyl)-5-2-(Methylthio)Ethyl-2-Thiobarbiturate
COMPOUND 25398 (Eli Lilly)		Na 1-Methyl-5-Allyl-5-(1-Methyl-2-Pentynyl) Barbiturate
DOLITRONE (Merrell)		5-Ethyl-6-Phenyl-M-Thiazane-2, 4-Dione

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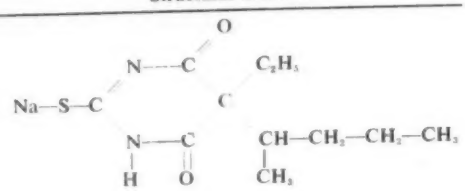
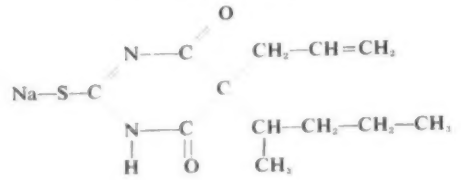
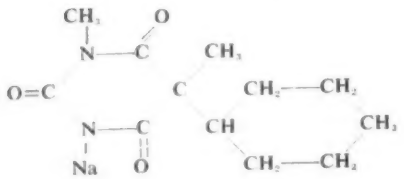
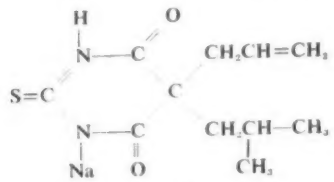
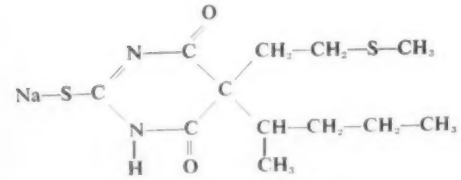
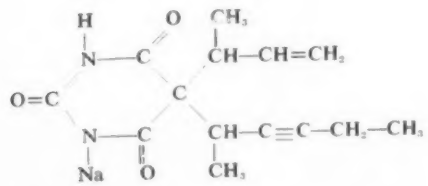
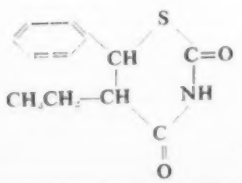

[facing page 194

according to the literature and manufacturers' data, are listed in table II. We have also listed the pH of 2.5 per cent freshly prepared solutions in distilled water (pH 6.7) as used in our tests. Our inability to corroborate the low alkalinity of Neraval should be carefully noted.

TABLE II
pH of Solutions

	Available data*	Our findings†
Thiopentone (Pentothal)	10.6	10.43
Thiamylal (Surital)	10.8–10.95	10.49
Hexobarbitone (Evipal)	10.6–11.21	11.16
Buthalitone (Transithal)	10.5 (10%)	10.45
Methitural (Neraval)	9.3–9.8	10.35
Compound 25398	10 –11	11.3
Dolitrone	11.4–12	10.93

* All are manufacturers' data with the exception of Neraval (Boone et al., 1956; Fitzpatrick et al., 1956). pH varies within the ranges indicated according to concentration and solvent.
† 2.5 per cent solutions in distilled water at 25°C.

For the sake of simplicity we shall throughout this paper refer to these agents by their official approved names as listed in table I, except for those compounds which have not yet been given one. Transithal is known as Baytenal in the U.S.A. and Germany. Pentothal is also known as Intraval in the U.K., Trapanal in Germany, Farmotal in Italy; Penthiobarbital, Thionembutal and Nesdonal are other synonyms. Neraval is Thiogenal in Germany. Evipal and Evipan (U.K. and Germany) are synonymous.

METHOD OF STUDY

Experiments were carried out on five subjects, all of whom were young, healthy males. All were submitted to seven tests each, one for each drug studied. The average interval between each test was one week.

On the morning before the first experiment, plasma volume was determined by the use of radio-active iodinated human serum albumin (albumin I 131; RIHSA Abbott), and a haemotocrit determination was carried out. From these the total blood volume was estimated.

Having had no nourishment for at least six hours, the subjects were admitted to the recovery room at least one hour before the experiment. At this time their height and weight were recorded. No premedication whatsoever was administered.

At the start of each experiment, a No. 18 Riley needle was inserted into the brachial artery, a No. 18 needle was inserted into the median basilic vein, and another intravenous needle with a Gordh needle mount was inserted into a vein on the opposite arm. The arterial and venous needles were connected to Statham strain gauges and arterial and venous blood pressures were directly observed on the screen of a six channel recorder, together with the electrocardiogram. Continuous permanent photographic tracings were made of these recordings.

The subject then breathed into a recording spirometer filled with oxygen and provided with a carbon dioxide absorption canister filled with fresh baralyme. After respiration appeared to be stabilized, RIHSA 50 to 75 microcuries was injected intravenously and radioactivity noted by means of a scintillation counter placed over the outflow tract at the left second interspace immediately adjacent to the sternum. From the resultant curve, cardiac output was calculated.

After recording all baseline values, the intravenous agent to be examined was injected. The sequence of drugs used was arranged by previously prepared random assignment for each volunteer in order to control the possibility of tolerance effects despite the interval of one week between tests. If such a tolerance effect did exist it would not manifest itself to the same degree in the same drug but the effect would be spread over all agents. All intravenous agents were freshly prepared 2.5 per cent solutions and were injected at the rate of 1 ml (25 mg) in approximately 1.5 seconds until the individual closed his eyes. After a short pause the sleep dose thus determined was repeated with moderate rapidity. Immediately upon completion of the injection, another cardiac output study was done by means of albumin-bound I 131. Respiration, arterial and venous blood pressures and electrocardiogram were continuously recorded from the moment of injection until the completion of the experiment. This point was considered to have been reached when the subject opened his eyes upon verbal command.

Great care was taken during the experiment to maintain absolutely unobstructed respiration

which, in most instances, was achieved without the use of an oral or nasal airway. One of these, however, was inserted if maintenance of a clear airway proved difficult. No endotracheal tubes were used. Apnoea following induction was permitted to persist for one minute. After one minute the subject's lungs were ventilated by compression of the chest until spontaneous respiration resumed.

Upon completion of the experiment, the individuals were returned to the recovery room, where they were permitted to rest until full recovery had taken place. Meanwhile, their rate of recovery, the presence of headache, diplopia, return of normal gait and their individual impressions of the agent were all recorded.

RESULTS

The vital statistics of the five subjects, including age, height, weight, body surface area, plasma volume and total blood volume are listed in table III. All five were roughly of the same age. The body surface area of three subjects was average for individuals in that age group; it was above average for the other two.

I. General Findings.

Dose.

The double sleep doses required for each subject and for each drug are listed in table IV. Since there appears to be a marked individual variation for the same agent, the dose as related to body surface area was calculated (table V). This table shows that, although the individual variation is considerable, it is not as pronounced as if the dose alone were considered. The total dose was also related to total blood volume (table VI). This does not always parallel dose per body surface area. The averages as listed in these three tables would seem to indicate that thiopentone and thiamylal are very similar in potency, with buthalitone by far the least potent agent milligram for milligram. Compound 25398 is the most potent. The other agents in line of increasing potency would appear to be methitural, dolitrone and hexobarbitone, with methitural closest to thiopentone and thiamylal.

Sleep patterns.

Anaesthesia was entirely smooth in all instances with both thiopentone and thiamylal, except that

TABLE III

Vital statistics

Subject	Initials	Age	Height (in)	Weight (lb)	Body surface area (sq.m)	Plasma vol. (ml)	Total blood vol. (ml)
1	A.B	22	68	150	1.8	3380	5630
2	L.C.	25	71	175	2.01	3560	6180
3	W.H.	23	68	162	1.85	3210	5460
4	N.K.	23	71	195	2.1	3660	6245
5	D.S.	23	71	145	1.86	4100	7100

1 inch = 2.5 cm. 1 lb = 0.45 kg.

TABLE IV

Dose (milligrams)

	1	2	3	4	5	Average
Thiopentone	850	1000	800	700	600	790
Thiamylal	800	800	900	800	600	780
Hexobarbitone	1000	950	950	875	1000	955
Buthalitone	1000	1000	1000	1000	1400	1080
Methitural	S.D.	800	700	850	700	762.5
Compound 25398	500	450	500	500	450	480
Dolitrone	800	1000	1000	750	1000	910

S.D. = Sleep dose only.

TABLE V

Dose/Body Surface Area (mg per square metre)

	1	2	3	4	5	Average
Thiopentone	472	497.5	432	333	322.5	411.5
Thiamylal	444	398	486	381	322.5	406
Hexobarbitone	555.5	473	513.5	417	538	499
Buthalitone	555.5	497.5	540.5	476	753	564
Methitural	S.D.	398	378	405	376	389
Compound 25398	278	224	270	238	242	250
Dolitrone	444	497.5	540.5	357	538	475

S.D. = Sleep dose only.

TABLE VI

Dose/Total Blood Volume (mg per 100 ml)

	1	2	3	4	5	Average
Thiopentone	15.1	16.2	14.7	11.2	8.5	13.1
Thiamylal	14.2	12.9	16.5	12.8	8.5	13.0
Hexobarbitone	17.8	15.4	17.4	14.0	14.1	15.7
Buthalitone	17.8	16.2	18.3	16.0	19.7	17.6
Methitural	S.D.	12.9	12.8	13.6	9.9	12.3
Compound 25398	8.9	7.3	9.2	8.0	6.3	7.9
Dolitrone	14.2	16.2	18.3	12.0	14.1	15.0

S.D. = Sleep dose only.

subject 2 exhibited after both drugs very slight spontaneous movements of the foot as anaesthesia became lighter towards the second half of the experiment.

Hexobarbitone. Although moderately satisfactory on the whole, was accompanied by spontaneous, often jerky, movements of the extremities in all instances. Subjects 4 and 5 exhibited a short period of generalized spasticity after completion of the injection which, after a short period, was followed by general relaxation. Crowing occurred in subject 1 and periodic respiration in subject 2.

Buthalitone. Anaesthesia was smooth in two instances (subjects 2 and 3). In subject 1 anaesthesia was complicated by violent coughing, spontaneous movements, excessive salivation and swallowing early during the anaesthesia, as well as partial obstruction due to cord spasm. All these resolved after a while and anaesthesia then was smooth. Cough, spontaneous movements and jerking of the legs were also observed in subject 5, while subject 4 exhibited hiccough and crowing, followed by marked spontaneous movements.

Methitural. Only four administrations were analyzed because subject 1 moved spontaneously during injection of the single sleep dose, dislodging the intra-arterial needle, so that the experiment had to be discontinued. Anaesthesia was smooth in one case (subject 4). Subject 2 had violent spasmodic cough at the end of the injection which necessitated the temporary administration of oxygen for one minute; this was followed by relatively smooth anaesthesia except for some cough as well as forced expiration and inspiration which made airway maintenance somewhat difficult. Subject 3 had violent coughing, spontaneous movements and wheezing with stridor and cyanosis, irregular jerky respirations, and later there was marked struggling and salivation. Spontaneous movements of arms and legs and groaning were experienced with subject 5.

Compound 25398 was the most unsatisfactory from the point of view of smoothness of anaesthesia. There was not one single smooth breathing pattern, all showing jerky respiration with crowing, twitching, marked spontaneous movements and respiratory obstruction at the level of the vocal cords (figs. 1 and 2). Respiration, as a rule, was laboured; there was hiccough in one instance and unexplained early cyanosis in another. All

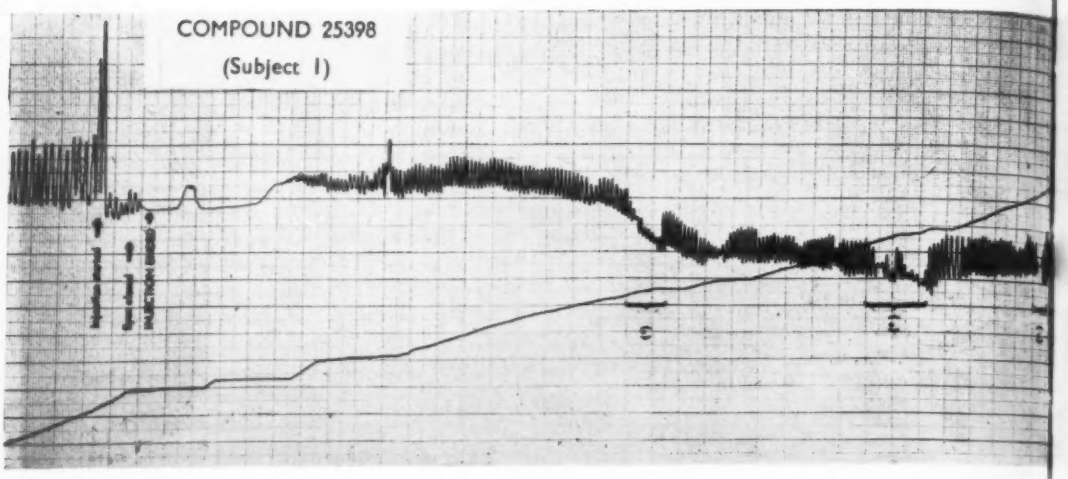

FIG. 1

Respiratory tracing for Compound 25398 showing marked irregularity of respiration. Asterisks denote episodes of respiratory obstruction due to cord spasm. Large square represents 20 seconds (horizontal) and 300 ml (vertical).

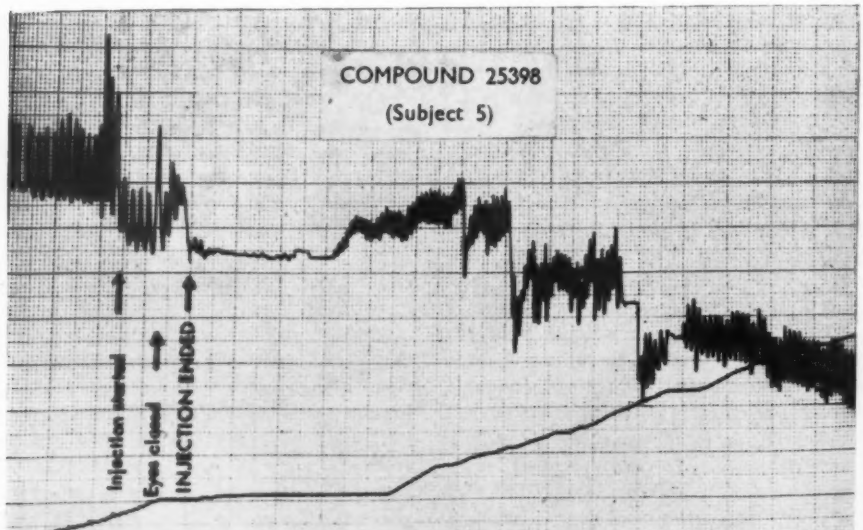

FIG. 2

Another respiratory tracing after Compound 25398 showing marked irregularity of breathing with episodes of respiratory obstruction due to cord spasm. (Scale as in fig. 1.)

these manifestations were so marked that great anxiety was experienced by the investigators during each administration.

Dolitrone. Anaesthesia was entirely smooth in one instance, but there was some twitching of the arms followed by sighing in two cases and mild spontaneous movements in two cases, and subject 5 exhibited laboured respiration throughout.

Wakening time.

Table VII shows again the very marked individual variations for the same drug from subject to subject. With one exception, subject 1 seemed to reach the end point of the experiment always later than all others and, in the instance of thiopentone and thiamylal, the discrepancy was very marked indeed. Averages for wakening time seemed to indicate that thiopentone (30 minutes) and thiamylal (28 minutes) are again very similar and produce the longest sleep time, whereas buthalitone shows the shortest average of only 7 minutes. Next in line with 11 minutes are hexobarbitone and Dolitrone while methitural and Compound 25398 hold intermediary positions with 14.5 and 20 minutes respectively.

TABLE VII
Wakening time

	1	2	3	4	5	Average
	min sec	min sec	min sec	min sec	min sec	min
Thiopentone	95 35	26 0	10 0	16 18	5 30	30
Thiamylal	70 0	35 0	15 10	15 2	6 0	28
Hexobarbitone	8 16	18 29	6 20	10 0	11 50	11
Buthalitone	11 30	7 20	3 10	9 5	4 35	7
Methitural	S.D.	35 3	8 25	6 0	8 20	14.5
Compound 25398	30 0	24 0	14 31	13 50	16 10	20
Dolitrone	13 25	13 48	6 15	11 20	12 7	11

S.D. = Sleep dose only.

Postanaesthetic manifestations.

All subjects experienced prolonged drowsiness, unsteadiness and hangover after thiopentone and thiamylal and, in a majority of cases, diplopia was also experienced when the individuals tried to focus. The postanaesthetic period with hexobarbitone was very satisfactory, most subjects being entirely rational and lucid very soon after wakening. They made such comments as "I feel tremendous" or "Never felt so good". The same quick awakening and absence of hangover were noticeable with buthalitone and methitural except that subject 3 was very wild and excited immediately on wakening from methitural. He then had a period of coughing, whereupon he fell into a secondary sleep and required some time to awaken therefrom. This was a case where marked stridor, some cyanosis and cough were experienced during the anaesthesia, and it may well be that the postanaesthetic manifestations were due to the resultant hypoxia. Despite the tremenduous difficulties of maintaining anaesthesia with Compound 25398, wakening was smooth, and the subjects felt quite well afterwards. There was some evidence of euphoria but no dizziness, nausea or emesis. Awakening after Dolitrone was likewise fast and smooth.

II. Cardiovascular Responses

Average systolic blood pressure, diastolic blood pressure, pulse pressure and pulse rate have been calculated for the average duration of anaesthesia for each agent. No electrocardiographic changes were observed in any of the experiments. Cardiac output and venous pressures will be the subject of a further report (Dobkin and Wyant, 1957).

Table VIII shows the average pre-anaesthetic blood pressures and pulse rates of all five subjects for each agent. Since the same individuals were involved in each experiment one would expect control values to be very similar. Only for hexobarbitone was the pre-anaesthetic average blood pressure elevated as compared with the other averages. Almost all subjects exhibited pre-anaesthetic tachycardia, which was most marked

TABLE VIII
Average Pre-anaesthetic vital Signs

	Thiopentone	Thiamylal	Hexobarbitone	Buthalitone	Methitural	25398	Dolitrone
Blood pressure mm Hg	119/72	121/72	137/75	126/68	119/75	124/70	121/78
Pulse rate/min	106	93	95	100	88	99	88

preceding the thiopentone administration. These data must be borne in mind in interpreting average percentage variations after administration.

Systolic blood pressure (fig. 3). All agents showed an immediate postinjection fall of systolic blood pressure lasting from 20 seconds (Dolitrone) to 2 minutes (methitural). Only in the case of hexobarbitone did this initial drop persist unchanged throughout the experiment. In no case was the drop less than 10 per cent. It was between 10 and 20 per cent for thiopentone, thiamylal, buthalitone, methitural and Dolitrone. The initial systolic blood pressure fall exceeded 20 per cent in the case of hexobarbitone and Compound 25398. With the exception of hexobarbitone, the systolic blood pressure after the initial fall rose, but this was almost insignificant for four of the agents, ranging between 2 and 4 per cent. Dolitrone showed the most significant rise from the initial depression since within 3 minutes from the end of injection the blood pressure reached a 4 per cent depression from an initial fall of 18 per cent, and after a further 3 minutes the depression of systolic pressure was only 2 per cent. The return of systolic blood pressure for Compound 25398, from 28 per cent of normal to 11.5 per cent of normal, took 2 minutes, but later two further drops occurred. The irregularity of the tracing for Compound 25398 must be interpreted in the light of movements, coughing and partial respiratory obstruction from cord spasm, all of which occurred with every administration.

If the findings for hexobarbitone are adjusted to a pre-anaesthetic average pressure similar to that preceding the other compounds (broken line), the percentage depression for hexobarbitone likewise falls between 10 and 20 per cent and is equal to that of thiopentone after the initial drop.

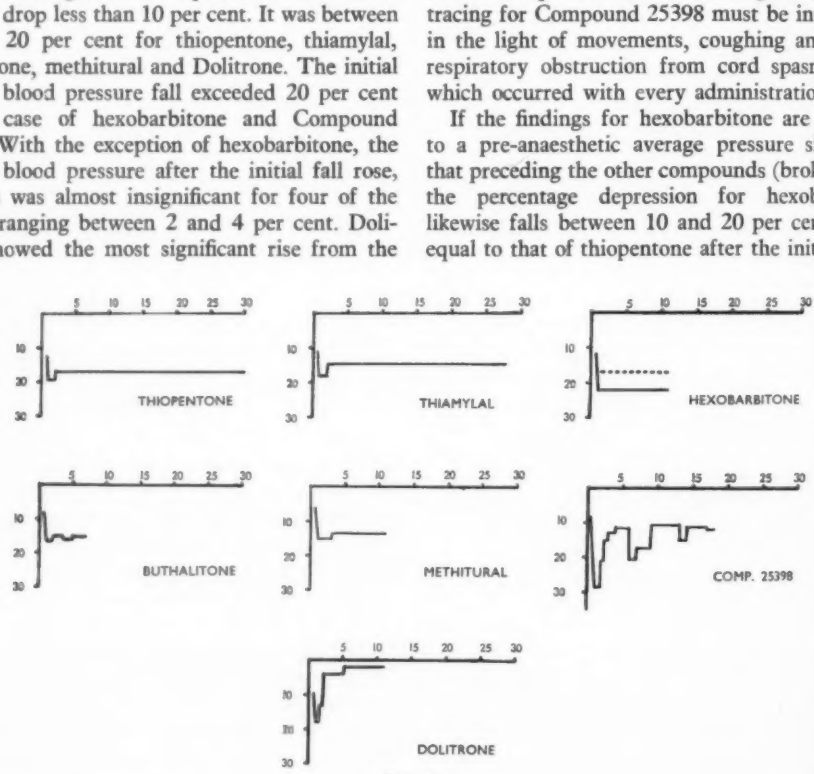

FIG. 3

Average systolic blood pressures. Broken line for hexobarbitone represents corrected values (see text). Abscissa: time in minutes. Ordinate: percentage of pre-anaesthetic control.

Diastolic blood pressure (fig. 4). Diastolic blood pressure also fell in every instance and was in all cases between 10 and 20 per cent. With methitural a further very slight drop of diastolic pressure to below 20 per cent occurred 2 minutes later; with hexobarbitone no change resulted after the initial drop for the remainder of the experiment. Within a short period of time, both Dolitrone and Compound 25398 showed a very significant rise of diastolic pressure, which soon rose above pre-anaesthetic levels. In interpreting the findings for Compound 25398, the previously mentioned technical difficulties must be borne in mind. In the remaining three compounds (thiopentone, thiamylal and buthalitone), a slight rise of diastolic blood pressure occurred after the initial drop, but only in the case of buthalitone did this bring the depression to less than 10 per cent of pre-anaesthetic values.

Pulse pressure (fig. 5). Immediate postanaesthetic drop in pulse pressure was least for methitural (less than 10 per cent), and after two minutes the pulse pressure returned to pre-anaesthetic values. The initial fall in pulse pressure for thiamylal reached 20 per cent; it was between 20 and 30 per cent for buthalitone and Dolitrone; it was 30 per cent for thiopentone; and it exceeded 30 per cent for hexobarbitone and Compound 25398. The depression of pulse pressure was maintained without any change for hexobarbitone, was significantly reduced for thiopentone, and was very significantly reduced within 5 minutes for Dolitrone. The subsequent rise for thiamylal amounted to only 5 per cent, but buthalitone showed a continuous diminution of pulse pressure for the first 5 minutes to 23 per cent of normal. The initial fall for Compound 25398 was very significant indeed, reaching 45 per cent; in the course of the next 5 minutes it rose in a step-ladder-like fashion to 10 per cent of normal. The initial fall, being uncomplicated by technical difficulties, is probably valid, but all subsequent findings must be interpreted with caution.

Pulse pressure again was adjusted for average pre-anaesthetic values in the case of hexobarbitone, which is indicated by the broken line. After correction, the pulse pressure values for hexobarbitone are similar to those for thiopentone after the initial drop.

Pulse rate (fig. 6). The least change of pulse rate occurred with methitural, being practically insignificant. Buthalitone is the only other agent which showed an elevation not exceeding 10 per cent. Thiopentone and thiamylal showed an eleva-

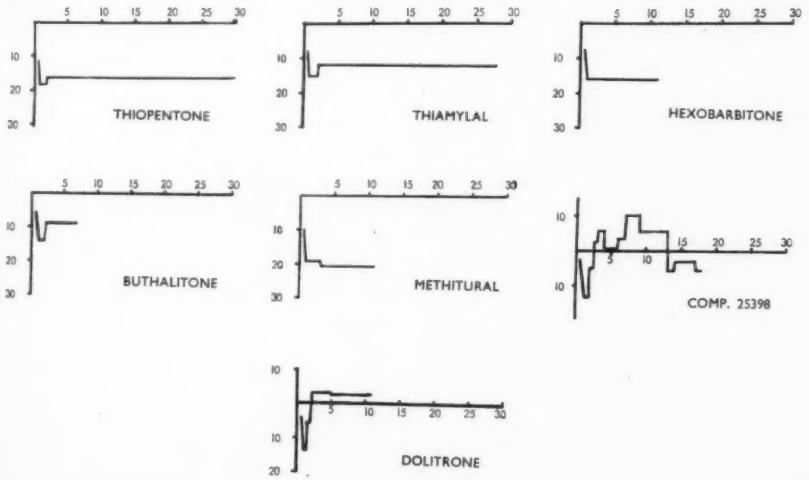

FIG. 4

Average diastolic blood pressure. Abscissa: time in minutes. Ordinate: percentage of pre-anaesthetic control.

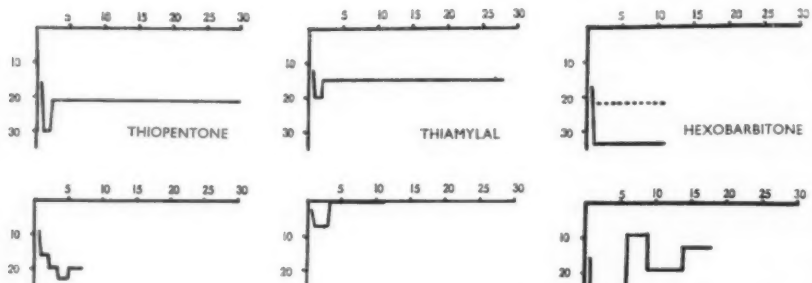

FIG. 5

Average pulse pressures. Broken line for hexobarbitone represents corrected values (see text). Abscissa: time in minutes. Ordinate: percentage of pre-anaesthetic control.

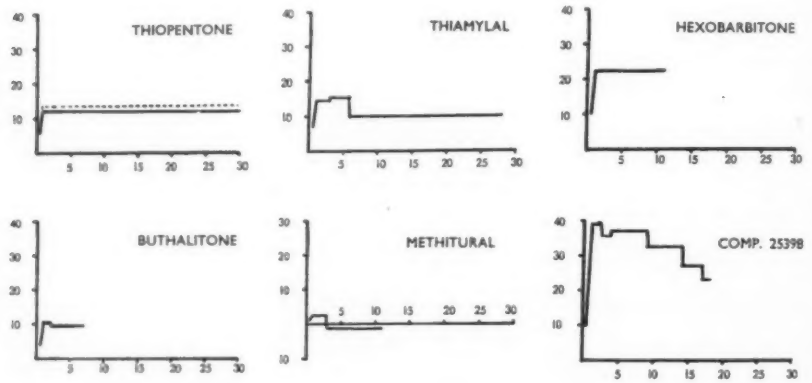

FIG. 6

Average pulse rates. Broken line for thiopentone represents corrected values (see text). Abscissa: time in minutes. Ordinate: percentage of pre-anaesthetic control.

tion of pulse rate exceeding 10 per cent. This elevation was maintained with thiopentone; with thiamylal it returned after 5 minutes to a level very similar to that of thiopentone. The elevation of pulse rate for hexobarbitone exceeded 20 per cent and was maintained at this level throughout. The initial tachycardia with Dolitrone reached 38 per cent but was maintained at this level for only 30 seconds and then gradually fell to an eventual increase of 18 per cent above normal. For Compound 25398, the initial rise was to almost 40 per cent for 90 seconds, whereupon a very gradual decrease to a final level of 23 per cent above normal occurred.

As stated previously, the pre-anaesthetic average pulse rate for thiopentone was higher than for all other agents (table VIII). Values have been corrected for an average pulse rate and are indicated by the broken line.

with an average apnoea of 87 seconds, showed by far the longest period of apnoea.

The most significant feature for thiopentone was the fact that four out of five subjects showed a short period of apnoea lasting a few seconds during injection, succeeded by a few breaths of a reasonably adequate tidal volume, and followed by the main apnoea after completion of the injection (figs. 7 and 8). After thiamylal it occurred only once. Delayed single apnoea occurred once with hexobarbitone, once with buthalitone and twice after Compound 25398.

Tidal volumes. Figure 9 shows the average tidal volumes for the five subjects for the average duration of anaesthesia. With thiopentone, thiamylal and Dolitrone it was relatively easy to compound these averages because respiratory patterns were moderately regular and breath-to-breath variations stayed within reasonable limits. For

TABLE IX
Apnoea (seconds)

	1	2	3	4	5	Average
Thiopentone	60	48	42	30	10	38
Thiamylal	70	60	—	—	16	29
Hexobarbitone	8	8	34	—	—	10
Buthalitone	60	6	18	—	16	20
Methitural	S.D.	—	—	—	10	2.5
Compound 25398	98	*	112	74	64	87
Dolitrone	—	12	54	—	45	22

S.D. = Sleep dose only. * Unsatisfactory tracing.

III. Respiratory Responses

Apnoea (table IX). Tidal volumes of less than 40 ml were considered to constitute a state of apnoea when they followed immediately upon a period of cessation of respiration. Again marked individual variations were noted for each agent. Averages seem to indicate that by far the shortest average period of apnoea occurred after the injection of double the sleep dose of methitural (2.5 seconds), with hexobarbitone (10 seconds) next in line. Buthalitone and Dolitrone are similar with 20 and 22.2 seconds respectively. The average period of apnoea with thiamylal was 29 seconds and only two of the five subjects became apnoeic at all. The average time of apnoea for thiopentone was 38 seconds, each subject becoming apnoeic following the injection. Compound 25398, methitural some difficulty in averaging was encountered for the first and second minutes following apnoea, but thereafter respiratory patterns were reasonably smooth. With hexobarbitone, buthalitone and Compound 25398, we met with considerable difficulty in calculating averages because of the wider variations in tidal volume from breath to breath. The values obtained and charted must therefore be interpreted in that light. After Compound 25398 irregular tracings were due to airway difficulty because of laryngospasm, coughing, breath holding, etc., in contrast to the irregular breathing patterns after hexobarbitone which occurred in the presence of a free airway. Wavy lines are used in order to indicate this difficulty in calculating averages. Two tracings for buthalitone showed such irregular breathing

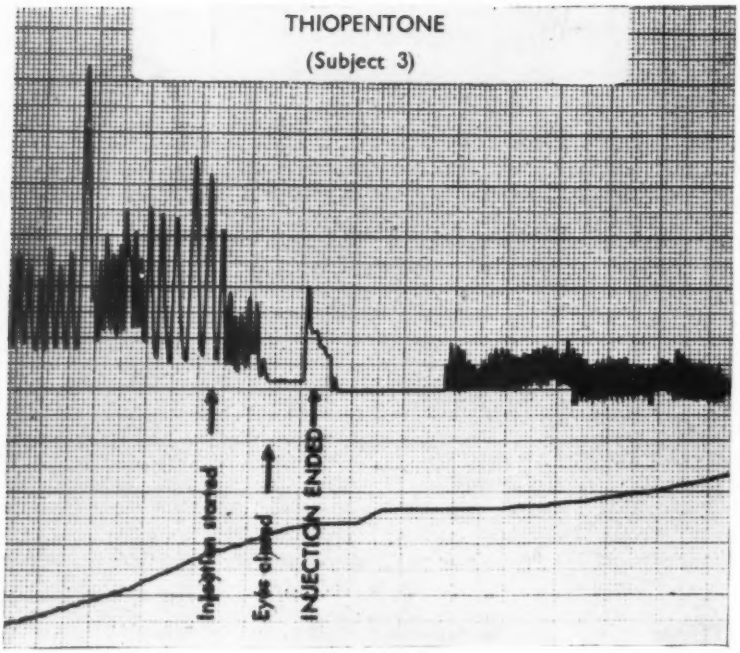

FIG. 7
Respiratory tracing for thiopentone showing double apnoea with first episode during injection. (Scale as in fig. 1.)

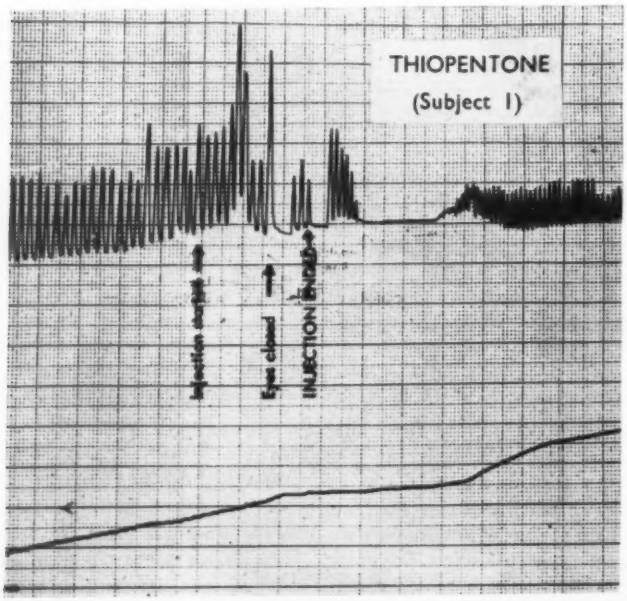

FIG. 8
Respiratory tracing for thiopentone showing triple apnoea, the first during injection, the second immediately following end of injection and main period of apnoea 46 seconds later. (Scale as in fig. 1.)

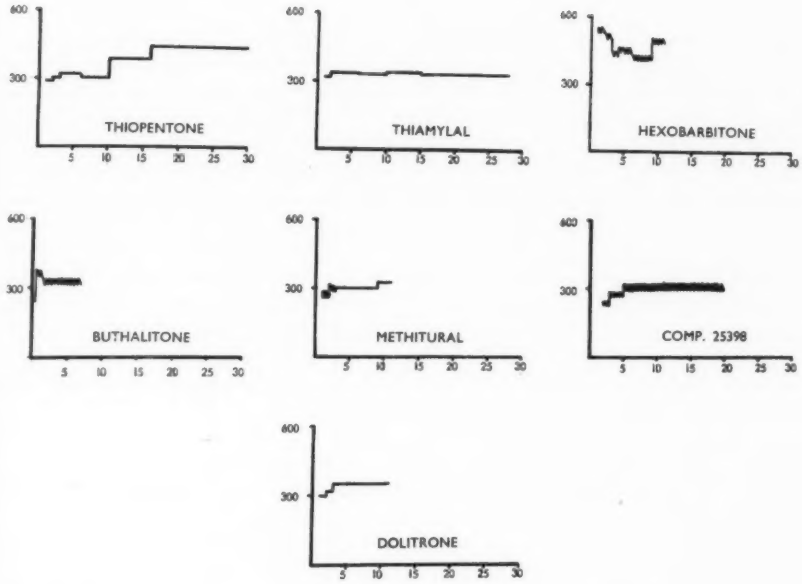

FIG. 9
Average tidal volumes. Abscissa: time in minutes. Ordinate: ml of air. Wavy lines denote irregular breathing patterns (see text).

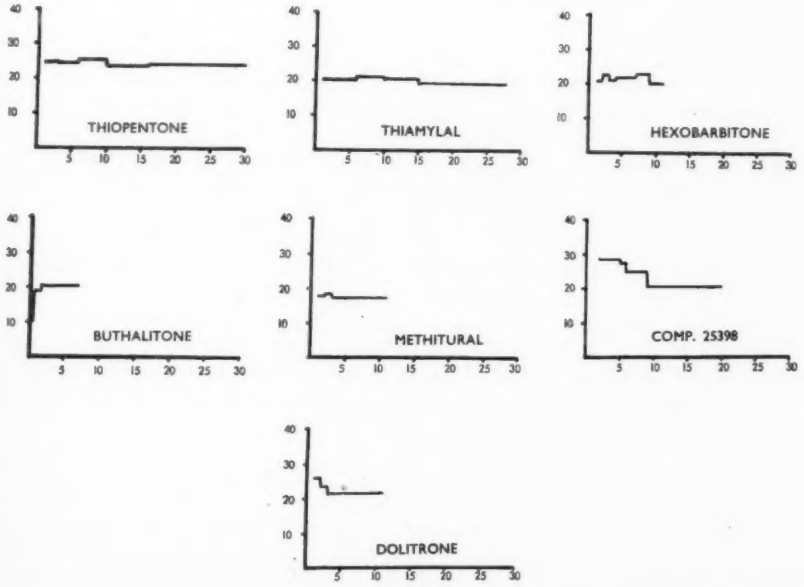

FIG. 10
Average respiratory rates. Abscissa: time in minutes. Ordinate: respirations per minute.

patterns due to coughing that they could not be included in the calculation of averages. With the exception of hexobarbitone, where tidal volumes were rather large following induction of anaesthesia, all other agents averaged 300 ml (or slightly more) per breath initially. Only thiopentone showed a significant increase of tidal volume after 10 minutes from the end of the injection.

Respiratory rate. Averages for respiratory rate are charted in figure 10. A respiratory rate of 18 to 22 per minute was obtained for all agents, with only Dolitrone and Compound 25398 showing initially a slight degree of tachypnoea.

Minute volume. The minute volume was calculated from tidal volume and rate. Averages are shown in figure 11. Methitural gave the lowest minute volume (because of the slow respiratory rate), but the average of slightly above 5 litres per minute is an acceptable value. All other agents gave a minute volume of over 6 litres per minute. Thiopentone showed the most marked increase (to over 10 litres per minute) 16 minutes after the end of injection. The tidal volume following injection of hexobarbitone averaged 10 litres per minute with an initial ventilation of more than 11 litres per minute. This large minute volume is probably an expression of the marked irregularity of respiration throughout the period of observation.

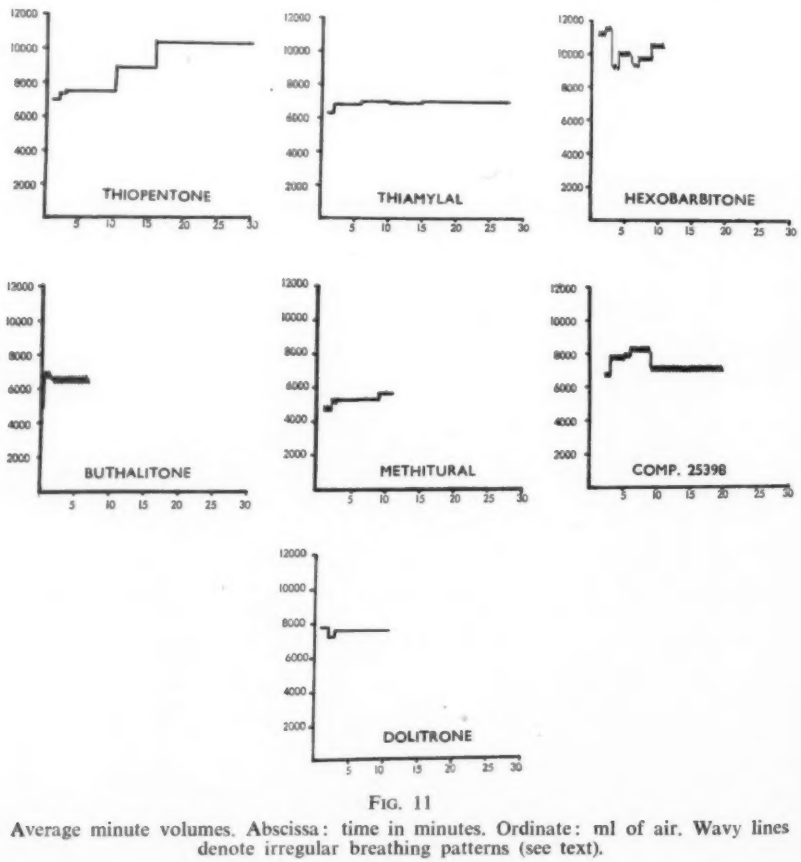

FIG. 11

Average minute volumes. Abscissa: time in minutes. Ordinate: ml of air. Wavy lines denote irregular breathing patterns (see text).

DISCUSSION

When considering the results obtained in a study of this kind, it must be borne in mind that, despite all precautions, two important factors cannot be controlled. The first of these variables is the degree of pre-anaesthetic apprehension which may exist to a greater or lesser degree. Some degree of control was hoped for by varying the sequence of administration of the various drugs for each subject, since it was assumed that apprehension would be greatest before the first experiment. However, when the average blood pressure and pulse rate of the subjects for each drug were calculated, there was an appreciable difference. Theoretically these averages should have been identical, inasmuch as they involved the total anaesthetic experience of the same individuals. One of the reasons for this discrepancy may have been either occasional difficulty in placing the intra-arterial needle or other technical difficulties before the start of the experiment. The second variable which could not be controlled was the state of wakefulness or tiredness of the individuals at the time of any given experiment. On one or two occasions it was related afterwards that the subject had had a late night and felt rather tired before the beginning of the experiment, which had its invariable repercussions in the dose requirement and the duration of postanaesthetic sleep. These two variables could only have been controlled if a much larger number of subjects were studied than we were able to procure for this series. Unfortunately, this is impossible in projects of this type.

One further difficulty in our study has been the determination of an end point. The end point was determined, quite arbitrarily, as the instant the patient first opened his eyes on verbal command. In two instances (once after buthalitone and once after methitural), the subjects related that they had heard the command but simply could not be bothered to obey. Therefore, in these two instances our conclusions as to the duration of anaesthesia are erroneous by one or two minutes to the disadvantage of the agent. Incidentally, it is worth noting that this occurred with a different subject in each instance. One further point requires emphasis: for the sake of uniformity of the experiment we used a standard concentration, namely 2.5 per cent. This is markedly more dilute than the recommended 10 per cent for buthalitone and 5 or 10 per cent for hexobarbitone; it is much more concentrated than the recommended 1 per cent for Compound 25398. This difference in concentration may well influence smoothness and duration of anaesthesia.

From the results previously discussed it becomes at once obvious that six of the drugs tested can be separated into two groups. One group consists of thiopentone and thiamylal, and the other of hexobarbitone, buthalitone, methitural and Dolitrone.

Thiopentone and thiamylal.

In double the sleep dose, which is markedly in excess of clinical doses used for induction of anaesthesia alone, these two agents are far from ultrashort acting. Both produce a transitory hypotension and diminution of minute volume which seem to return to more acceptable levels more promptly with thiopentone than with thiamylal. On the other hand, postinduction apnoea was, on the average, shorter with thiamylal than with thiopentone and the occurrence of apnoea itself was less consistent with thiamylal. Both agents were characterized by prolonged postoperative drowsiness, lack of co-ordination, diplopia and hangover. Maintenance of anaesthesia with both of these agents was invariably quite smooth.

The very frequent occurrence of double apnoea with thiopentone is of interest. It probably represents a redistribution of the drug following the primary impact of injection.

Hexobarbitone, buthalitone, methitural and Dolitrone.

In double the sleep dose, these four agents may truly be described as ultrashort acting with very much prompter awakening than after the first group and a conspicuous absence of the postanaesthetic phenomena observed after the administration of thiopentone and thiamylal. Average apnoea was by far the shortest after methitural, was longest after buthalitone (20 seconds), and intermediate after hexobarbitone. Against these undoubted advantages, it should be noted that entirely smooth anaesthesia was the exception rather than the rule, with spontaneous movements,

cough and hiccough being the most prominent complications. Few of these complications were of sufficient intensity, however, to disturb markedly the progress of the anaesthesia. Our use of buthalitone 5 and 10 per cent (in clinical practice) would tend to confirm the frequent presence of undesirable muscular activity even in that concentration. This has, on occasion, been rather disturbing to the surgeon, although it was never severe enough to interfere with the procedure at hand. The relatively frequent occurrence of these phenomena with methitural under clinical conditions has also been described (Boone et al., 1956; O'Herlihy et al., 1956). Of the four agents under consideration, hexobarbitone produced the relatively greatest cardiovascular and respiratory changes and must therefore be considered the least suitable agent in this group.

Compound 25398.

Compound 25398 was definitely an unsatisfactory drug when used as a 2.5 per cent solution. Smooth maintenance was entirely impossible in all instances, coughing, cord spasm and muscle twitching being the outstanding phenomena. Because of this marked interference with respiration, cyanosis was common and this may well be reflected in the prolonged wakening time. It is surprising, therefore, that no unpleasant post-anaesthetic sequelae were noted. This agent also showed two instances of delayed apnoea, several minutes after the completion of the injection. The average apnoea time was by far the longest of all agents tested.

In a small clinical series, using a 1 per cent solution, anaesthesia was usually smooth and the agent compared very favourably in this respect with the other intravenous agents under discussion. However, even with a single sleep dose, apnoea is very much more prolonged than with other drugs, lasting about one minute after the administration of 150 to 200 mg of the compound. The smooth awakening and the absence of hangover which were noted in the experimental work have been confirmed in clinical practice.

CONCLUSIONS

Thiopentone and thiamylal have been found to be thoroughly predictable agents. They show, however, a marked prolonged effect in the relatively large doses used.

Hexobarbitone, buthalitone, methitural and Dolitrone are all markedly shorter acting, even in large doses, but it would appear that for the shorter duration one must pay the price of less smooth and more uneven anaesthesia, a price which we see no justification in exacting under normal operating room conditions. Because of its more detrimental effects, especially on respiration, hexobarbitone cannot be recommended. Dolitrone, despite its satisfactory performance in this study, must be excluded because of its unpredictability and tendency to cause phlebitis on which we have elaborated elsewhere (Wyant et al., 1956). Buthalitone and methitural seem to have a place mainly in outpatient practice where, for the sake of quick awakening and absence of disorientation post-operatively, it may be advisable to accept the handicap of spontaneous movements, hiccoughs, etc. For induction of longer anaesthesia, where duration of the induction agent is usually of secondary importance, we should hesitate to recommend an agent which so frequently gives minor trouble.

Compound 25398 must never be administered in a 2.5 per cent solution. The drug gives fairly smooth and short-lasting anaesthesia when administered in the 1 per cent solution and awakening is relatively prompt and free from side effects, even after repeated injections. The agent has the disadvantage of prolonged apnoea in whatever concentration it is used. Compound 25398 seems to be worthy of further study.

SUMMARY

Seven intravenous anaesthetic agents have been compared in five subjects under controlled conditions, each subject receiving double the sleep dose of each agent at weekly intervals.

The total dose required as well as cardiovascular and respiratory responses have been evaluated.

It is concluded that, in the relatively large doses used, thiopentone and thiamylal are not ultra-short acting agents. They have almost identical properties, as has also been reported by others (Tovell et al., 1955). Of the true short acting agents, methitural and buthalitone show the great-

est promise, although they frequently do not give entirely smooth anaesthesia. The implications of this are discussed.

Compound 25398 is not to be administered in concentrations greater than 1 per cent. Its greatest disadvantage seems to lie in unduly long post-induction apnoea.

ACKNOWLEDGMENTS

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Supplies of drugs were kindly made available by the following firms: sodium thiopental (Pentothal(R)) by Abbott Laboratories, Montreal; thiamylal sodium (Surital(R)) by Parke, Davis and Company Ltd., Walkerville, Ontario; hexobarbital sodium (Evipal(R)) by Winthrop Stearns Inc., New York; methitural sodium (Neraval(R)) by Schering Corporation, Montreal. P.Q., buthalitone sodium (Transithal(R)) by Poulenc Ltd., Montreal, P.Q.; Compound 25398 by Eli Lilly and Company, Indianapolis, Ind.; and MRD–125 (Dolitrone(R)) by the Wm. S. Merrell Company, Cincinnati, Ohio, U.S.A.

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REFERENCES

Boone, J. D., Muñoz, R., and Dillon, J. B. (1956). Neraval Sodium: A New Ultra-Short-Acting Thiobarbiturate: Preliminary Clinical Investigations. *Anesthesiology*, **17**, 284.

Dobkin, A. B., and Wyant, G. M. (1957). The Physiological Effects of Intravenous Anaesthesia in Man. *Canad. Anesth. Soc. J.* (in press).

Fitzpatrick, L. J., Clarie, D'A. C., and Mersch, M. M. (1956). Methitural Sodium (Neraval(R) Sodium): A New Ultrashort Acting Intravenous Anesthetic. *Anesthesiology*, **17**, 684.

O'Herlihy, D. B., Nishimura, N., Little, D. M. jr., and Tovell, R. M. (1956). The Clinical Usage of Neraval. *Canad. Anesth. Soc. J.*, **3**, 326.

Tovell, R. M., Anderson, C. C., Sadove, M. S., Artusio, J. F. Papper, E. M., Coakley, C. S., Hudon, F., Smith, S. M., and Thomas, G. J. (1955). A Comparative Clinical and Statistical Study of Thiopental and Thiamylal in Human Anaesthesia. *Anesthesiology*, **16**, 910.

Wyant, G. M., Kilduff, C. J., Merriman, J. E., and Dobkin, A. B. (1956). Evaluation of Dolitrone. *Canad. Anesth. Soc. J.*, **3**, 295).

BOOK REVIEW

Lumbar Puncture and Spinal Analgesia (2nd edition). By Sir R. R. Macintosh. Published by E. and S. Livingstone Ltd. Pp. 150; illustrated. Price 25*s*.

It is somewhat unexpected, in view of the present disinclination of British anaesthetists to use spinal anaesthesia, but nevertheless very encouraging that Sir Robert Macintosh should think it worth while to bring out a second edition of his book on Lumbar Puncture and Spinal Analgesia. The fact that spinal analgesia has produced, and no doubt can produce again, results at least as good as that of any other technique for those operations for which it is suitable has generally been lost sight of. The reason for this was stated in the preface to the first edition; it is not due to the greater number of accidents with spinal analgesia than with general anaesthesia, but to the fact that these latter are successfully hidden in the grave.

This second edition is almost unique among second editions in that it is somewhat shorter than the first, an example that might well be followed by others. For the student attempting lumbar puncture, for whom this book is primarily written, there is no better book and as far as my experience goes, not one so good.

It is hardly necessary to write that this is as beautifully illustrated as others from the same source.

E. Falkner Hill

Brit. J. Anaesth. (1957), **29**, 210

DENTAL TRIAL OF CARBOCAINE

A New Local Anaesthetic

BY

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A RECENT report from Scandinavia (Dhunér et al., 1956) describes a clinical trial of Carbocaine in which 652 cases were injected with results which the authors describe as raising " expectations that Carbocaine may prove to be of great value as a local anaesthetic drug." It was found that, when no adrenaline was used, anaesthesia lasted longer with Carbocaine than with lignocaine (Xylocaine), for ½, 1 and 2 per cent solutions. Using adrenaline, anaesthesia lasted longer with lignocaine. However, none of the above cases was for dental operation. This paper describes a trial of the drug in dental cases and gives the results obtained.

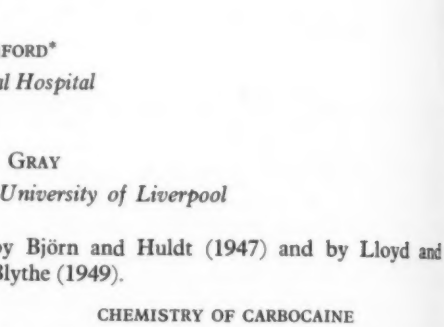
It is considered that a search for new local anaesthetics is necessary because, although lignocaine is a great improvement on earlier local anaesthetics, clinical experience shows that it does not provide consistently successful anaesthesia. Sherman, Fiasconaro and Chilton (1954) obtained complete elimination of pain in 84 per cent of cases with lignocaine 2 per cent plus epinephrine 1 : 50,000, and in 88 per cent of cases with lignocaine 2 per cent plus epinephrine 1 : 100,000.

It must be remembered that although Björn (1947) and Huldt (1953) obtained 100 per cent success with lignocaine, they worked only on upper lateral incisors and tested anaesthesia by Björn's (1946) electrical method, not by surgery.

Also patients sometimes complain that the injection makes their faces or lips feel swollen, hard, cold, too numb, or that the anaesthesia is " too dense ". Attention has been drawn to this by Björn and Huldt (1947) and by Lloyd and Blythe (1949).

CHEMISTRY OF CARBOCAINE

Carbocaine is d, 1-N-methyl-pipecolic acid 2, 6-dimethylanilide and has the structural formula (Ekenstam and Egner):



The base is poorly soluble, but the hydrochloride is easily soluble in water and very resistant to acid and alkaline hydrolysis.

PRELIMINARY TRIAL

Two per cent Carbocaine without adrenaline was first tried in 65 dental cases for both regional and infiltration anaesthesia in order to obtain some idea of the following factors:

(1) Dosage. This must be sufficient to give reasonable success, but 100 per cent success must not be obtained, as a smaller concentration or volume might still produce 100 per cent success.
(2) The time between injection and anaesthesia.
(3) The frequency of anaesthesia.
(4) The duration of anaesthesia.
(5) The depth of anaesthesia.
(6) Any adverse effects, e.g. prolonged numbness of the soft tissues.

* Work carried out under a grant received from the Bofors Co., Karlskoga, Sweden.

The results of the preliminary trial were similar to those to be given for the blind testing trial which followed and, therefore, need not be detailed.

MAIN TRIAL

Blind Testing.

The need for blind testing in the study of drugs is well established. The drugs, which were 2 per cent Carbocaine and 2 per cent lignocaine, each without adrenaline, were prepared in 21 bottles containing 0.1 per cent chlorocresol and labelled with a code number. The key to this code was not revealed to the operator until the end of the trial.

Operator.

All the injections were done by one operator, thus eliminating variations of technique, etc.

Patients.

These were both male and female, from 11 years of age upwards, who were undergoing a course of treatment in the department of operative dentistry of this university. These patients are usually both intelligent and co-operative and are preferable to " casual " patients in this respect. In all cases anaesthesia of permanent teeth was investigated.

Dosage.

2.3 ml (35 minims) were given for regional anaesthesia; 1.7 ml (25 minims) were given for infiltration anaesthesia.

Method of Determining Onset of Anaesthesia.

The operation was started, and only when the patient experienced pain was the injection given. This was considered important, because it eliminated two sources of error:

(1) Anaesthesia might occur whilst the bur was still in enamel. The dentine would then be insensitive when reached, but the exact time of anaesthesia would not be known.

(2) The tooth, for physiological or pathological reasons, might be insensitive even without an injection. If the injection had been given first such a case would have been wrongly classified as a successful anaesthesia. It is interesting to note that 11 such cases occurred during this trial. They were, of course, excluded.

An injection was given rapidly in 5–10 seconds and the time was noted to the nearest quarter-minute. A revolving bur was applied to the dentine at short intervals and the time at which complete anaesthesia occurred was noted to the nearest quarter-minute. In many cases partial anaesthesia was experienced before this time, but only the time of onset of complete anaesthesia was recorded.

It should be noted that anaesthesia to probing and excavating was sometimes present when there was not anaesthesia to the bur.

Termination of Anaesthesia.

Cavity preparation was continued and the time was noted at which pain was again experienced. This gave the exact duration of anaesthesia. A period of partial anaesthesia often followed and this was sometimes adequate to permit continuation of the operation.

Each operation was done by a student. This was a real advantage because students work much more slowly than do those who are qualified. It was, therefore, often possible to determine the exact termination of anaesthesia. Nevertheless, in many cases the operation on dentine was concluded whilst anaesthesia was still present. This time was noted and gave the minimum period of anaesthesia.

It would have been statistically more convenient to be able to determine the exact end of anaesthesia in every case. This could have been achieved by decreasing the dose, but such a step would have decreased the number of successful anaesthesias, which would not be giving the patients fair consideration.

Termination of Soft Tissue Symptoms.

These are usually described as " numbness ", " fatness ", " coldness ", etc. It is desirable to reduce the duration of these as much as possible. The time of termination was obtained by asking the patient to complete a stamped addressed postcard. The results are only approximate, for the accuracy depends on the patient's interest, observation and energy.

Successful Injection.

An injection was regarded as successful if anaesthesia occurred within 10 minutes. This is an arbitrary time but it is regarded as generous because a dentist usually only allows 30 minutes or even less for his appointments. The injection

was also regarded as successful no matter how short the duration of anaesthesia. It is important to note this fact, because an operator would not normally regard an anaesthetic as successful if it failed to cover the entire period of the operation. However, this objection is overcome by presenting the results for the duration of anaesthesia as well as for the percentage of successful injections.

Anaesthesia of Dentine when the Pulp is still Sensitive.

In this investigation anaesthesia was determined for the dentine only. It was sometimes found that the dentine was anaesthetized when the pulp (accidentally exposed by a student operator) was not. This has also been noticed by Björn (1947).

Regional Anaesthesias.

These were divided into inferior dental nerve injections which were administered for the lower molars, and posterior superior dental nerve injections which were administered for the upper second and third molars.

Infiltration Anaesthesias.

These were used for all other teeth. However, the upper central incisor was excluded from the test because it usually needs an injection on each side of the midline and it is not permissible simply to add the two doses.

The upper first molar sometimes requires two injections, although, in this project, it was given only one infiltration injection. It is therefore considered in a group by itself.

Hydrogen Ion Concentration.

The pH of the Carbocaine solution was 6.5 whilst that of the lignocaine was 5.4. It is generally considered that the more acid the solution the longer will it take to dissociate in the tissues with release of the anaesthetic base. Theoretically, therefore, the Carbocaine in this trial had a slight advantage over the lignocaine as regards the time of onset of anaesthesia. Practically, however, this is probably not the case. Tainter, Throndson and Moose (1939) and Tainter (1941) showed that there is little or no advantage in rendering the solutions alkaline as regards onset, duration, dose and incomplete anaesthesia. According to Björn and Huldt (1947), "the efficiency of a neutral Xylocaine-adrenaline solution was found to be essentially the same as for that of an acid (pH=5) Xylocaine-adrenaline solution." Later they stated that "the effect of both, therefore, can safely be compared to that of the acid (pH=5) procaine solution." In 1953, Huldt found that "for Xylocaine + epinephrine, the hydrogen ion concentration (within the range pH 4–7) is of no practical importance to the efficiency." He considered that "had the experiments been performed with lower concentrations of Xylocaine (than 1 ml 2 per cent and 1 ml 1 per cent) it is possible that a difference might have shown up."

On the other hand, Brynholf (1947) found that "A 2 per cent procaine-adrenaline solution . . . with pH 7.34 gave a shorter analgesia latency than the same solution with pH 4.85 and with pH 3.61. It also gave longer duration of the analgesia than the same solution with pH 3.61."

However, the differences in pH used by Brynholf were very much greater than those concerned in the present investigation. It was therefore considered that a valid comparison could be made between the two solutions concerned.

RESULTS

Successful Anaesthesias.

Table I details, under each anaesthetic, the number of successes as judged by the above criteria. It will be observed that of the 126 injections of lignocaine, 48.3 per cent resulted in anaesthesia, whereas of 87 injections of Carbocaine, 82.8 per cent were effective. This difference is significant as also is the difference in success rate between the two drugs for both infiltration and regional anaesthesias.

Onset of Anaesthesia.

Table II is an analysis of the times of onset of anaesthesia with the two drugs and it can be seen that there is no significant difference between the drugs in this respect. The numbers of cases are obviously smaller as only the successful injections could be assessed for time of onset.

Duration of Anaesthesia.

The number of patients in which the duration of anaesthesia could be accurately measured was smaller still, as many left the operating room before recovery of sensation. However, it was possible to estimate the duration of anaesthesia in 74 patients

TABLE I

TABLE I
Effectiveness of Anaesthesia

Type of anaesthesia	Lignocaine: Details of patients No.	M.	F.	Average age	% Success	Carbocaine: Details of patients No.	M.	F.	Average age	% Success	Significance of difference
Infiltration of *6*	12	8	4	19.9 (12–38).	16.7	7	3	4	15.7 (12–20)	71.4	Insufficient cases
Infiltration of $\frac{2345}{12345}$	46	23	23	24.1 (12–51)	30.4	39	19	20	20.4 (12–49)	76.9	Significant difference $p>0.05$
Regional: Inferior dental	45	19	26	20.3 (11–44)	70.1	32	15	17	21.3 (12–42)	87.5	? Significant $p>0.06<0.05$
Regional: Posterior superior dental	17	9	8	18.8 (11–30).	58.9	9	7	2	17.6 (12–29)	100	Significant difference $p>0.01$
All cases	120	59	61	21.9 (11–51)	48.3	87	44	43	20.1 (12–49)	82.8	Significant difference $p>0.01$

TABLE II
Time of Onset of Anaesthesia.

Type of anaesthesia	Lignocaine: Details of patients No.	M.	F.	Average age	Time of onset (minutes)	Carbocaine: Details of patients No.	M.	F.	Average age	Time of onset (minutes)	Significance of difference
Infiltration of *6*	2	2	–	19 (12–38)	3.5	5	2	3	15.6 (12–18)	2.6	Insufficient cases
Infiltration of $\frac{2345}{12345}$	14	7	7	24.8 (13–51)	2.4 ± 0.36	30	15	15	22.3 (12–49)	2.51 ± 0.30	Not significant
Regional: Inferior dental	32	12	20	20.8 (11–44)	2.92 ± 0.29	28	13	15	21.5 (12–42)	3.44 ± 0.45	Not significant
Regional: Posterior superior dental	10	4	6	20.7 (12–30)	2.46 ± 0.39	9	2	7	17.6 (12–29)	2.22 ± 0.28	Not significant
All cases	58	25	33	20.7 (11–51)	2.73	72	32	40	20.8 (12–49)	2.84	

TABLE III

Duration of Anaesthesia.

Type of anaesthesia*	Cases in which actual duration of anaesthesia was measured				All cases: including those in whom the duration of anaesthesia was greater than that of operation†			
	Lignocaine		Carbocaine		Lignocaine		Carbocaine	
	No. of cases	Average duration (min)	No. of cases	Average duration (min)	No. of cases	Average duration (min)	No. of cases	Average duration (min)
Infiltration of $\frac{2345}{12345}$	12	13.8 ± 2.9	20	15.7 ± 0.9	13	15.9	29	15.3
Regional: Inferior dental	18	25.9 ± 1.5	10	28.6 ± 3.0	31	29.3	26	28.8
Regional: Posterior superior dental	9	14.7 ± 2.7	4	18.7 ± 5.4	10	16.9	7	21.3
Total	39	19.5 ± 1.6	34	19.5 ± 1.9	54	21.2	62	21.9

* Infiltration of *6* not included, because of small number of cases.

†Duration of anaesthesia in cases not in lefthand column is taken as duration of operation (which was always less than actual anaesthesia).

and from the lefthand columns of table III it can be seen that the two drugs gave very similar results.

The series with each drug were comparable in respect of age and sex distribution, but for the sake of clarity these details are not shown.

If the remaining cases, in which only the minimum anaesthesia was determined, were also included, the results obtained (righthand columns of table III) confirm that the drugs give a similar length of time of anaesthesia.

Duration of Soft Tissue Symptoms.

The duration of soft tissue symptoms was determined in a very much smaller number of patients and again no difference between the two drugs was demonstrable (table IV).

TABLE IV

Duration of Soft Tissue Symptoms.

Type of anaesthesia	Lignocaine		Carbocaine	
	No. of cases	Average duration (min)	No. of cases	Average duration (min)
Infiltration of $\frac{2345}{12345}$	3	66	18	84
Regional: Inferior dental	14	113	22	130
Total	17	105	40	109

DISCUSSION

The results show that, as regards the percentage of successful anaesthesias, carbocaine (82.8 per cent) was decidedly superior to lignocaine (48.3 per cent). This low percentage with lignocaine may be compared with the results of Huldt (1953). He used Björn's (1946) method and obtained the results given in table V. Because of the different methods and dosage it is not possible to compare closely his results with those obtained in the present investigation, but it is interesting to see that they are somewhat similar.

TABLE V

Percentage of successful anaesthesias with Lignocaine without Adrenaline (after Huldt, 1953)

Dose of lignocaine	No. of subjects	Incidence of anaesthesia
2 ml 1%	25	16%
2 ml 2%	25	60%
1 ml 2%	20	60%
1 ml 4%	12	75%

In view of the greater effectiveness of Carbocaine it might be combined with smaller concentrations of adrenaline and might possibly prove more effective as an anaesthetic than lignocaine. This was not done in this trial, as interest was directed to the relative effectiveness of the two drugs alone.

It should be borne in mind, however, that the work of Ekenstam et al. (1956) on caudal anaesthesia suggests that the duration of anaesthesia with Carbocaine is not as proportionately prolonged by the addition of adrenaline as it is with lignocaine.

SUMMARY AND CONCLUSIONS

A new local anaesthetic, Carbocaine, has been compared with lignocaine, using the blind testing method. Adrenaline was not added.

It was found that, under the conditions described, Carbocaine gave 82.8 per cent and lignocaine 48.3 per cent of successful anaesthesias.

There was no significant difference as regards onset, duration or soft tissue symptoms.

It is suggested that further research on this anaesthetic might well prove valuable.

ACKNOWLEDGMENTS

We must express our gratitude to Dr. J. W. Dundee, for his very considerable help in the statistical aspects of the trial; to the students and patients in the Liverpool Dental Hospital; and Mr. Alstead, the Dispenser of the Liverpool Royal Infirmary, for making up the blind solutions.

REFERENCES

Björn, H. (1946). Electrical excitation of teeth and its application to dentistry. *Svensk. tandlak. Tidskr.*, **39**, suppl.

—— (1947). The determination of the efficiency of dental local anaesthetics. *Svensk. tandlak. Tidskr.*, **40**, 771.

—— Huldt, S. (1947). The efficiency of Xylocaine as a dental terminal anaesthetic compared to that of procaine. *Svensk. tandlak. Tidskr.*, **40**, 831.

Brynolf, I. (1947). An investigation on the effect of 2 per cent procaine-adrenaline solutions with varying pH and salt content. *Svensk. tandlak. Tidskr.*, **40**, 868.

Ekenstam, B., Egner, B., Ulfendahl, L. R. Dhuner, K. G., and Oljelund, O. (1956). Local trials with Carbocaine: a new local anaesthetic drug. *Brit. J. Anaesth.*, **28**, 503.

Huldt, S. (1953). Factors influencing the efficiency of dental anaesthetics in man. *Acta. odont. scand.*, **11**, 13.

Lloyd, R. S., and Blythe, J. O., jr. (1949). Clinical experiences with lidocaine as a local anaesthetic. *J. Amer. dent. Ass.*, **39**, 296.

Sherman, H., Fiasconaro, J. E., and Chilton, N. W. (1954). A comparison of the clinical effectiveness of the higher potency local anaesthetics in operative dentistry. *J. Amer. dent. Ass.*, **48**, 151.

Tainter, M. L. (1941). Summary of studies on optimal composition of local anaesthetic solutions. *Anesthesiology*, **2**, 489.

—— Throndson, A. H., and Moose, S. M. (1939). Alleged clinical importance of buffered local anaesthetic solutions. *J. Amer. dent. Ass.*, **26**, 920.

CORRESPONDENCE

CITRATE INTOXICATION FOLLOWING RAPID MASSIVE BLOOD TRANSFUSION

Sir,—Dr. Argent does well to draw attention to the complicated subject of citrate intoxication in the March issue of the Journal. Investigators and clinicians in America have been interested in this subject during the last few years (Bunker et al., 1955; Smith, 1956; Hubbard et al., 1956; Bunker, 1957).

The fall in the level of ionized calcium with consequent upset in the calcium/potassium ratio is responsible for the cardiac depression seen in citrate intoxication. In this condition the picture would, ordinarily, be that of gradually diminishing contractions ending in asystole. Ventricular fibrillation, as in the case described by Dr. Argent, is unusual.

The article does not mention the controversy over the possible effects of low ionized calcium levels on the bleeding time. Although calcium is often given in the hope of decreasing haemorrhage, most authorities (Bunker et al., 1956; Goodman and Gilman, 1955) doubt if calcium deficiency is ever responsible for prolonged bleeding time.

Citrate intoxication is particularly likely to occur when there is liver disease or interference with hepatic circulation. It should be remembered that if the body is unable to ionize or metabolize the citrate it is unlikely to be able to ionize adequately or metabolize the gluconate. Calcium chloride, a rapidly dissociated source of ionized calcium (Goodman and Gilman, 1955), is the drug of choice in acute calcium deficiency.

Calcium replacement is not without its risks and should be performed cautiously. It is particularly dangerous in digitalized patients, as the digitalis effect may be potentiated (Gold and Edwards, 1927). It is difficult to gauge the exact amount of calcium required when citrate intoxication is diagnosed or suspected. A dose of 2 to 3 ml of 10 per cent calcium chloride given slowly, intravenously, repeated at intervals of a few minutes until the blood pressure and, when the heart is visible, the cardiac contractions are improved, has given a satisfactory response on several occasions. Calcium therapy should certainly be considered when massive transfusion is likely, especially in the presence of liver disease.

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REFERENCES

Bunker, J. P. (1957). Citric acid intoxication. *Anesth. Analg.*, **36**, 83.

Bunker, J. P., Stetson, J. B., Coe, R. C., Grillo, H. C., and Murphy, A. J. (1955). Citric acid intoxication. *J. Amer. med. Ass.*, **157**, 1361.

Gold, H, and Edwards, D. J. (1927). Effects of ouabain on the heart in the presence of hypocalcemia. *Amer. Heart J.*, **3**, 45.

Goodman, L. S., and Gilman, A. (1955). *The pharmacological basis of therapeutics*, 2nd ed., p. 810, New York.

Hubbard, T. F., Neis, D. D., and Barmore, J. L. (1956). Severe citrate intoxication during cardiovascular surgery. *J. Amer. med. Ass.*, **162**, 1534.

Smith, R. M. (1956). Blood replacement in thoracic surgery for children. *J. Amer. med. Ass.*, **161**, 1124.

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ANAESTHETIC ASPECTS OF BRONCHIAL FISTULA

BY

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SINCE the term bronchial fistula can, from the practical point of view, be applied to any abnormal connection between the inside of the intrathoracic respiratory system and the outside, it includes a very wide assortment of cases. Fistulae vary in their acuteness and duration from a few minutes up to thirty years or more (Huizinga and Smelt, 1950), and in their consequences from the rapidly fatal to the almost insignificant. Although the anaesthetic management of these cases falls mainly within the province of those working in specialized units, any anaesthetist may be caught unawares from time to time. Quite apart from this consideration the subject is well worth discussing because of its intrinsic interest and because it has probably called for as much anaesthetic ingenuity and resourcefulness as any other subject within the specialty.

AETIOLOGY

There are many ways in which a bronchial fistula may arise, but it is usually sufficient to bear in mind the commoner and more important ones. An empyema very frequently communicates with the bronchial tree and, conversely, a lung abscess sometimes opens into the pleura. In either of these cases there is a grave danger of pus flooding the respiratory tract. A lung cyst or an emphysematous bulla may burst and give rise to leakage of air from the lung, and in the case of a ruptured tuberculous cavity there is obviously danger from both these complications.

Accidental trauma to the chest may cause a bronchial tear or rupture, and the deliberate trauma of pneumonectomy or resection may result in a fistula, usually as a consequence of infection in the bronchial stump.

DIAGNOSIS

The diagnosis of bronchial fistula is surprisingly often in doubt, and therein lies one of its chief dangers to the anaesthetist. The features of the condition depend upon whether the chest is open or closed, and in the latter case upon whether the fistula is valvular or not. A valvular opening in a closed chest, for example, will allow air to enter the pleural space from which it cannot then escape, and the result is a tension pneumothorax, with dyspnoea, cyanosis, and displacement of the mediastinum to the opposite side. If the air is able to leak around the pleura as well, and into the mediastinum, the pneumothorax may not be severe, but there will be surgical emphysema, sometimes sufficient to blow up the whole body like the Michelin man of the advertisements. At the opposite extreme, a nonvalvular fistula in an open chest, for example in an old empyema which has been draining through a sinus or a tube for twenty or thirty years, will present no dramatic features at all, and the patient's only complaint may be that the noise of his air leak makes people think he is carrying a small animal in his coat pocket.

Various things may suggest the presence of a fistula, the coughing up of foul sputum in a case of empyema, for instance, especially with change in posture; or the persistent bubbling of a water seal drain postoperatively. There are various useful diagnostic tests which may be carried out. Firstly, if a pneumothorax is aspirated, in the absence of a fistula it is obviously possible to reach a stage at which practically all the air has been withdrawn, and the intrapleural pressures will then show a positive-negative swing approximating to the normal range. But, in the presence

of a communication between the bronchial tree and the pleura, the pneumothorax is constantly refilled from the lung, and it is possible to go on aspirating air indefinitely without ever producing a negative intrapleural pressure. Secondly, if a radio-opaque dye is put into the chest to replace aspirated fluid and outline the extent of a sinus, the appearance of a partial bronchogram is conclusive proof of the presence of a fistula (fig. 1), and conversely the same is true if lipiodol from a bronchogram appears in the pleural space. As an alternative to this test methylene blue may be injected into the pleura, and in the presence of a fistula it will often appear in the sputum. It is also interesting to remember, as Coope mentions, that because of the different rates of diffusion of oxygen and carbon dioxide in a self-contained pneumothorax, as opposed to one which communicates with a bronchus, it is possible to diagnose the presence of a fistula by gas analysis (Coryllos, 1937; Coope, 1951).

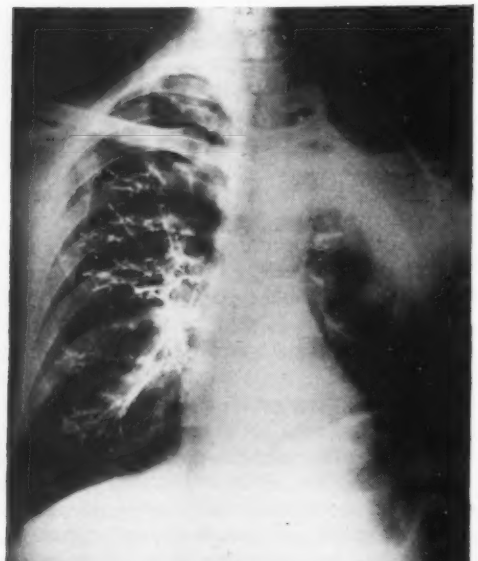

FIG. 1

Sinogram with lipoid following left upper lobectomy and thoracoplasty; the appearance of a complete right bronchogram demonstrates the presence of a fistula.

For convenience, the main causes and effects of different types of fistula are roughly summarized in table I.

TREATMENT

Once diagnosed, the treatment of a fistula depends on its cause, and need not be discussed in detail here. However, in many cases it is to assist in the treatment, by operation, that the anaesthetist is called upon to do his work. It should go without saying that every one of these cases must be assessed on its individual merits and fully discussed with the surgeon before anything is done.

The patient may come to theatre with a closed chest, or with an open drainage tube, or with an underwater seal drain, or with a " stoma ", which simply means a hole in the chest wall to facilitate drainage. In any case he should be accompanied by a postero-anterior and lateral X-ray of his chest taken not more than a few hours previously, and in the absence of these films he is best left severely alone. The first point in the anaesthetic management of these cases is to see just what is inside the chest in the way of fluid or pus, and just where it is; and in order to be of any value at all this information must be right up to the minute.

ANAESTHETIC PROBLEMS

The problems peculiar to these cases, from the anaesthetic point of view, may be grouped under two headings:

(1) Spillover of fluid.

(2) Leakage of air and gases:
   (*a*) to the outside;
   (*b*) into the pleural space.

Spillover of fluid.

The fluids most likely to enter a fistula are pus from an abscess or empyema, and blood from an operation site. Apart from the immediate mechanical danger of gross respiratory obstruction through blockage, with pus there is the danger of pneumonitis and pulmonary suppuration, and with blood there is the danger that once having entered the bronchial tree, which it may do quite silently, it will clot and be irremovable by suction (Mushin and Rendell-Baker, 1953).

TABLE I
Classification of Fistulae

	Cause	Type of fistula	Features
CONGENITAL	—	Tracheo-oesophageal.	Inhalation of feeds, etc.
TRAUMATIC	Direct injury.	Stove-in chest, fractured ribs with damaged lung.	Paradox. Haemopneumothorax.
	Direct injury.	Open chest with damaged lung or bronchus.	Paradox, mediastinal flap, haemorrhage, channelling.
	Direct or indirect blow.	Tear or rupture of bronchus in closed chest.	Pneumothorax, may be bleeding. Surgical emphysema.
	Exertion, straining. Inflation with excessive pressure.	Rupture of subpleural bleb, emphysematous bulla, lung cyst or tuberculous cavity, in a closed chest.	Pneumothorax, may be valvular, with tension. Danger of producing T.B. empyema.
	Operative:		
	(1) Adhesion sectn.	Air leak into closed A.P.	Haemopneumothorax.
	(2) Bronchotomy at opn.	Full bore bronchus leak in wide open chest.	Gross air leak, danger of blood and secretion entering bronchus.
	(3) Postop.	(1) Stitch hole leakage. (2) Bronchiolar fistula.	Persistent blow of drainage tube.
		(3) Frank B-P fistula. (4) Bronchiolar pocket.	Pyopneumothorax, with or without drain or stoma.
INFECTIVE	Empyema.	Bronchopleural, or long standing bronchocutaneous.	Cough. Foul sputum with posture.
	Lung abscess.	Rupture into bronchus in closed chest.	Danger of drowning in spillover.
	Subdiaphragmatic.	Bronchobiliary, etc. Closed chest.	Characteristic sputum.
NEOPLASTIC	Carcinoma, etc.	Bronchopleural, oesophageal or mediastinal, or postop.	Pneumothorax, may be bleeding or abscess, or surgical emphysema.

There are essentially three methods of guarding against spillover:

(1) Positive pressure.
(2) Posture.
(3) Occlusion and exclusion.

Magill (1936) pointed out that not only is positive pressure respiration justifiable in the presence of a fistula, which acts as a safety valve, but that it is also very useful as a means of preventing fluid from entering the bronchial tree. A constant outgoing stream of gases will tend to blow fluid away from the opening and keep it clean, and in practice this is a very satisfactory way of handling a small fistula in a relatively dry field. It is the method commonly adopted of necessity when a blocker has not been used and the surgeon inadvertently opens a bronchus with bleeding going on in the vicinity, and it may well be adopted from choice in selected cases.

Case 1. Mr. H. W. had a left upper lobectomy and corrective thoracoplasty in a Swiss sanatorium in 1953. He was seen in Cheshire in 1955, after he had started to cough up considerable quantities of sputum, and suspicion of a bronchopleural fistula was confirmed by chest aspiration and a methylene blue test. A stoma was made, and the patient did well; later he was admitted to the Chest unit in Liverpool to have his sinus widely laid open for skin grafting.

The patient was anaesthetized with thiopentone and suxamethonium; his larynx and trachea were sprayed with 4 per cent lignocaine and, after intubation, anaesthesia was maintained with nitrous oxide and oxygen and small supplements of thiopentone. There was a definite air leak, but the sinus was quite dry until, during the operation, considerable bleeding was encountered from branches of the cephalic vein. From

this time until the end of the operation the anaesthetist kept his hand on the bag, gently assisting the respiration and maintaining a slight positive pressure. No blood entered the bronchial tree.

The question of posture raises the theoretical possibility of two schools of thought, rather as in the case of acute intestinal obstruction. Either the patient must be tilted so that the fluid stays where it is, at the lowest point of the chest, or else he must be tilted to an extreme degree in the opposite direction so that fluid will drain through the trachea without spilling to the unaffected parts of the lungs. As a rule this latter method is impracticable and fraught with danger, and there is fairly general agreement on this point. It has been taught for years that rib resection for drainage of an empyema or abscess should be performed under local anaesthesia with the patient sitting up, to prevent spillover and drowning (Brock, 1952; Lee, 1953), and there is no doubt that, as Barrett tersely remarks, "this accident happens" (Barrett, 1950). Belcher and Grant (1955), in discussing the management of postoperative fistula, stress that on no account should postural drainage through the communicating bronchus be attempted as this will almost invariably lead to aspiration pneumonia. In practice, although the drainage position looks quite safe, there are two objections: firstly, the outpouring of pus can be so copious that by the time it is sucked out the patient is hopelessly anoxic, and secondly, there is an inevitable time interval while the positioning of the patient is going on, during which he is in an unsafe position. If the fistula is small, and the quantity of fluid in the chest is also small, it is reasonably safe to put the patient in the lateral position and maintain controlled respiration with a slight positive pressure, bearing in mind that if spillover does occur at any stage the table must immediately be tilted and effective suction instituted. In the presence of a large fistula and a chest full of fluid, to turn the patient into the lateral position with the affected side uppermost is asking for trouble.

The opposite principle of posturing, the anti-drainage principle, is often summarized by saying that the fistula must be kept above the fluid level (Mushin and Rendell-Baker, 1953). It will usually be the case that when the patient arrives in the theatre, in whatever position he may be, his fistula will be above his fluid level, and in the case of a fistula near the hilum, such as may follow pneumonectomy, for example, this must be so, or he would already be drowned. But it is not always either true or necessary that this should be the case; a patient with a large empyema and a fistula somewhere in the lower lobe may come to theatre sitting up, with his fistula submerged in pus, but he comes to no harm, and he will continue to be safe as long as his position is such that the communicating bronchus inclines upwards out of the fluid at a sufficient angle. It is, of course, dangerously misleading to interpret the dictum as meaning that the patient must be *arranged* so that the fistula is above the fluid level. In the example given above, for instance, this could be done by tilting the patient head down, but any such manoeuvre would almost certainly result in emptying the whole empyema into the bronchial tree.

As an alternative to the sitting position, which is inconvenient if the surgeon wishes to operate towards the back of the chest, the face down position may be used. The patient is rolled on to his face with the affected side passing underneath, and is then fixed in position with the chest at a slight angle so that the side to be operated on is still lower than the normal side. In this way a collection of pus in the lower chest can be prevented from spilling, especially if a head up tilt is also maintained throughout.

Although the following case is not one of bronchial fistula, it is a good illustration of the value of posture.

Case 2. Miss A. W., suffered from gross bronchiectasis of the left basal segments and lingula, and in spite of prolonged pre-operative postural drainage it was feared that secretion would be copious during resection of the affected segments. After induction with thiopentone and tubocurarine, bronchoscopy was performed in the supine position, and suction was carried out. With percussion of the left side of the chest during the bronchoscopy it was possible to remove a considerable quantity of sputum. A Magill tube was then passed, and anaesthesia continued with nitrous oxide and oxygen. The patient was turned into the face down position, with approximately a 30 degree head up tilt, and in this position the surgeon was able to secure the bronchi and vessels without disturbing the dependent position of the lower lobe and lingula. In spite of the fact that the lower lobe was virtually a bag of pus, there being a cavity in the anterior basal

segment 2.5 × 1.5 cm, no difficulty was experienced by the anaesthetist, and no secretion was aspirated during the operation.

The third method of avoiding spillover of fluid, the theoretically ideal method, is to block off the fistula in some way or exclude it from the rest of the bronchial tree. However, since this is also an important method of controlling air leak through a fistula, it will be more convenient to discuss it in that connection.

Leakage of air and gases.

The air leak through a fistula may be so slight that the anaesthetist is unaware of it until the surgeon points it out, or it may be so gross that with gas flows up to 20 l./min it is impossible to inflate the patient. If the chest is open the air leak results in channelling of gases along the line of no resistance, that is between the trachea and the fistula, with the result that the remainder of the lungs are underventilated, or not ventilated at all. This in turn has two consequences; firstly, hypoxia and carbon dioxide retention are inevitable, and secondly it is impossible to keep the patient asleep with an inhaled anaesthetic. The danger of explosion through leakage is considerably stressed in the literature (Hewer, 1944), but not many people nowadays regard an intact pleura as a reliable safeguard, so that in any chest case the use of diathermy with explosive agents is uncommon.

If the chest is closed, air leak through a fistula leads to a tension pneumothorax, with increasing cyanosis, and resistance to inflation. The mediastinum is displaced, and in the presence of spontaneous breathing shows a marked respiratory shift, the great veins are compressed and cardiac action is thus enfeebled. Once recognized this state of affairs is dramatically relieved by putting a needle into the chest. It should also be remembered that a distensible lung cyst can be blown up to a remarkable extent and can produce exactly the same picture in the absence of any fistula at all (Gray and Edwards, 1948).

Another occasional complication of air leakage is surgical emphysema, which may be alarmingly increased by positive pressure inflation. This sometimes happens also with rupture of the oesophagus when the patient is inflated with a face mask (Dundee, 1955; Schweizer and Howland, 1956).

In the management of air and gas leakage there are again three possible methods of approach:

(1) Spontaneous respiration.
(2) Controlled respiration with positive pressure.
(3) Occlusion and exclusion.

It has been mentioned that a patient may live for many years with a bronchial fistula and suffer relatively little inconvenience. In such cases the physiological effects of the lesion are minimized by pleural thickening and rigidity of the mediastinum, and the same can be said for many postoperative cases. With a fistula after pneumonectomy, for example, if the mediastinum is fairly fixed and the remaining lung is healthy, there is no reason to expect gross distress. With a good sized drainage tube to ventilate the empty hemithorax, or with a stoma, the patient is just as well off breathing through a bronchial stump as through his nose and mouth; he has in fact the advantage of a greatly reduced dead space, one better than a tracheotomy from the functional point of view, but regrettably inaccessible to the anaesthetist. In many cases of this kind there is everything to be said for letting the patient breathe spontaneously throughout the operation, provided he can be kept asleep. It is certainly the method of choice for the anaesthetist who is not an expert at manipulating blockers, and for small operations on the patient who is too ill to tolerate much instrumentation. If the chest is dry, the patient may be placed in any position which suits the surgeon's convenience. If there is pus in the chest and the operation is such that the patient must be in a position which threatens spillover, it is essential to block or exclude the fistula.

Case 3. This middle-aged man complained of haemoptysis, and chest X-ray showed shadowing of the right upper lobe suggestive of tuberculosis or neoplasm. Bronchoscopy was inconclusive, due to bleeding from the upper lobe opening, and a thoracotomy was carried out. This revealed a carcinoma for which an upper lobectomy was performed, but during the procedure bleeding into the bronchus was profuse and the anaesthetist was unable to cope with the situation in spite of a steep head down tilt. Bronchoscopy and suction were carried out, and the operation continued successfully. Postoperatively the patient did not do well, presenting a variety of

symptoms and signs which suggested a diagnosis of periarteritis nodosa. He was treated with cortisone, and shortly afterwards his bronchial stump broke down and left a full bore fistula of the right upper lobe bronchus. He was ill and emaciated, but his chest had been drained and was fairly dry. Intubation was performed under local anaesthesia, and nitrous oxide and oxygen were then administered with a high flow-rate, the expiratory valve being kept closed. By this means, with the occasional addition of a little trichloroethylene, it was possible to anaesthetize the patient sufficiently to enable the surgeon to open the chest and control the air leak. Suxamethonium was then given, and controlled respiration instituted, with a high flow of gases. The patient made a good recovery from the operation, but subsequently died.

Reference has already been made to the second method, controlled respiration with positive pressure. Magill (1936) pointed out that a fistula acts as a safety valve and renders positive pressure safe, and this technique is frequently used. With a large fistula it may be quite impossible to keep up with the leak, even with both oxygen and nitrous oxide by-passes down, but it is usually feasible to keep the patient going until the surgeon can stop the leak, or reduce it, with a pack.

Occlusion and exclusion.

It is now necessary to consider the question of bronchial occluders and endobronchial intubation. The idea of blocking off a diseased part of the lung, or excluding it from the rest of the respiratory tract, has caught the imagination of anaesthetists since the earliest days of major thoracic surgery. Gale and Waters (1931) discussed the use of one-lung anaesthesia; Magill did much work on it in the nineteen-thirties; and Nosworthy (1941), speaking of broncho-pleural fistulae in his classic paper on thoracic anaesthesia, described one-lung anaesthesia as the ideal method. It is widely appreciated among thoracic anaesthetists that to block off the lower lobe or the whole lung on either side is comparatively easy, but the upper lobes, and the right upper lobe in particular, present a much more difficult problem.

In a case of empyema or abscess, with a fistula in the lower lobe, spillover and air leak can be controlled quite simply by passing a bronchus blocker into the affected lower lobe bronchus under direct bronchoscopic vision (fig. 3a). The Vernon Thompson blocker is preferable to the Magill, being less likely to slip, but it should be remembered that neither is infallible in this respect. Two points about this procedure are worth stressing; firstly it must be performed without putting the patient into a position in which spillover can occur, and, secondly, the patient must not be allowed to become anoxic. If the patient is cyanosed to begin with, and has a large fistula, it is extremely dangerous to give suxamethonium and rely on inflating with oxygen; the value of this oxygen is negligible if it just blows straight out through the fistula, and if the chest is closed or the drainage tube is clamped off, there is the additional risk of producing a tension pneumothorax. There are no cases in which prolonged pre-oxygenation is more valuable than these, since it may offer the only hope of providing enough oxygen to last the patient until the blocker is in place: in the very ill, it is inadvisable to abolish or depress respiration even for one or two minutes, and the blocker should be placed in position under topical anaesthesia.

Postoperative fistulae present a special problem, because the bronchial stump is nearly always too short to hold a blocker of any kind.

After pneumonectomy there is nothing on the affected side into which to place a blocker, and the best way of dealing with such a case is to intubate the opposite side. With a left sided fistula, it is quite easy to pass a long Magill endotracheal tube into the right main bronchus and blow up the cuff at the carina. In this position the air leak is controlled, and the right upper lobe opening is not interfered with (fig. 2a).

Case 4. When this patient came to the theatre for a stoma operation following left pneumonectomy, he was thought to have a fistula. After induction with thiopentone and tubocurarine a long No. 10 Magill tube was passed blindly into the right main bronchus, and the cuff inflated. There was no air leak and nothing to be sucked out, and the anaesthetist began to doubt the existence of a fistula. At the end of the operation, however, atropine and neostigmine were given, and the trachea being quite dry, the cuff was deflated. The patient immediately woke up, coughed out his tube, and simultaneously the surgeon remarked that the fistula was blowing vigorously.

With a right sided fistula, the left main bronchus may be intubated either under vision with a Magill endobronchial tube, or blindly with a

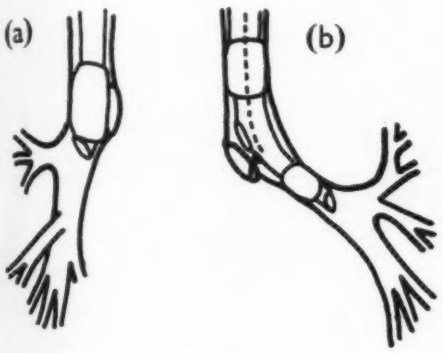

FIG. 2

Main Bronchus Fistulae

(*a*) Endotracheal tube in right main bronchus with cuff occluding fistula after left pneumonectomy. If the short bevel is cut in the plane shown, the right upper lobe opening need not be blocked.

(*b*) Carlens tube in use after right pneumonectomy, showing how right side of tube can be used for suction and drainage. Testing for leakage after repair of the fistula is possible by blowing gases down this right side lumen.

Carlens tube (fig. 2b) or an M-L tube (Macintosh and Leatherdale, 1955). Blind intubation of the left main bronchus with an ordinary Magill endotracheal tube is much more difficult and uncertain, and the danger of attempting it in these cases is that if the tube enters the wrong side it may go straight through the fistula into the empyema.

Case 5. This patient came to theatre for attempted closure of a bronchopleural fistula following a right radical pneumonectomy for carcinoma. He was given thiopentone and tubocurarine, and intubated; but on inflation it was found that the air leak was unmanageably large. Atropine and neostigmine were given, and the patient was maintained on nitrous oxide and oxygen and trichloroethylene, with spontaneous respiration. The repair was not successful, and some days later, in the ward, the patient turned on his left side, flooded his bronchial tree, and nearly died. A second attempt at closure of the fistula was therefore made. Under thiopentone-tubocurarine anaesthesia, a bronchoscope was passed, but the instrument immediately filled with pus from the fistula, and the situation got out of hand. An attempt was made to pass a Magill endotracheal tube blindly into the left main bronchus, but it entered the fistula and inflation was impossible. The patient was gravely anoxic, and the heart stopped beating. Intracardiac adrenaline was ineffective, and cardiac massage was quickly instituted. The heart started again, and the operation was rapidly completed with the Magill tube in the trachea.

Closure of the fistula was successful, and the following morning the patient was awake, but was aphasic, and had a paresis of the right arm. There is no doubt that he had irreversible damage to the central nervous system due to anoxia, and he died a few days later.

After lower lobectomy, a blocker can be placed in the main bronchus immediately above the fistula. Such a blocker will often occlude the the upper lobe opening, especially on the left side, and thus produce an unaerated upper lobe which will slowly collapse as the operation proceeds (fig. 3b). In spite of the theoretical disadvantage of arteriovenous shunting, this is a practicable method which has the advantage of safety. There should be no difficulty in inflating the upper lobe again at the end of the operation, and it may be recalled in this connection that Organe (1949) has described the technique of deliberately intubating the right side for cases of patent ductus. The important thing is that the blocker should be as low as possible; there must be no opening into the upper lobe (or middle lobe, if this remains) *below* the blocker, or else this lobe is very likely to be flooded (fig. 3c).

The problems associated with occlusion and exclusion are greatest in the case of a fistula following upper lobectomy. It is not possible to use a blocker in the main bronchus above the upper lobe opening, or perhaps partly occluding it, since this would leave the lower lobe open to the fistula and liable to be flooded (fig. 4a). The same objection applies to intubation of the opposite side, which is only justifiable if the chest is perfectly dry. Actual occlusion of the upper lobe opening may be attempted by packing with ribbon gauze, as in Crafoord's (1938) technique, although if this is done it is usually impossible to maintain an opening to the lower lobe (Halton, 1943); otherwise, it is necessary to use an endobronchial tube with a cuff to block the fistula, and side holes above this through which the opposite lung can be ventilated (fig. 4b) (Mansfield, 1947; Vellacott, 1954). For an upper lobe abscess, a special blocker, such as Mully's (1950) may be used, but after upper lobectomy the only blocker likely to be practicable is Halton's.

Case 6. Mr. A. A. had a right upper lobectomy for tuberculosis in 1954 followed by fistula. The danger of spillover was anticipated during repair of the fistula, and a suitable tube was improvised. A No. 8 Magill

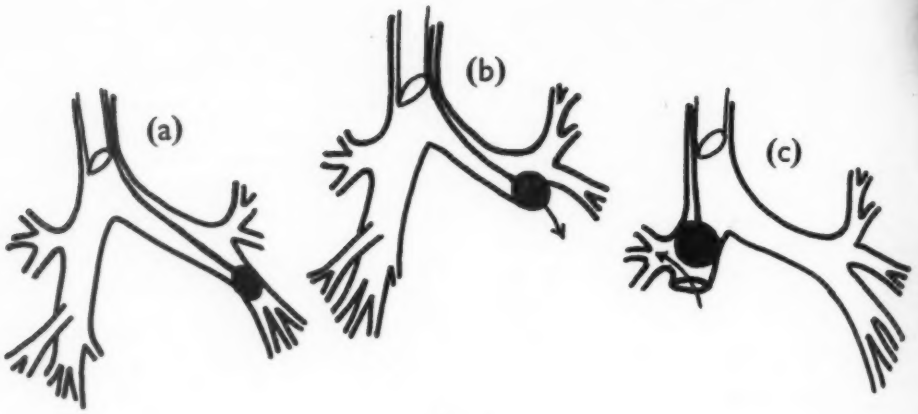

FIG. 3
Lower Lobe Fistulae

(*a*) Showing blocker in left lower lobe bronchus.
(*b*) After lower lobectomy, if the blocker is introduced too far it may pass through the fistula, or be dislodged by the surgeon.
(*c*) If the bronchial stump is short, the blocker will necessarily occlude the upper lobe opening. More serious than this is the danger that if the blocker is too high in position there will be flooding of the upper lobe behind it.
Depending on the position of the patient and the amount of fluid in the chest, it may be possible to rely on continuous suction through the catheter incorporated in the blocker to prevent this accident.

endotracheal tube with a short cuff was selected, and the distal end cut off with a slight bevel immediately beyond the cuff. Several holes of about ¼ inch diameter were cut in the tube above the cuff, around the circumference (it is not necessary for these holes to lie directly opposite the left main bronchial orifice; with a tube of this size there is enough space between the tube and the tracheal wall to allow ventilation of the left side without appreciable resistance). The whole tube was left rather long, and passed blindly into the right main bronchus. A second, detachable, cuff was fitted above the holes, to make an airtight fit in the trachea, so that controlled respiration could be used, and the operation proceeded without incident.

The patient's fistula subsequently broke down again, and he was readmitted to hospital in 1957 for a further repair. At this time the chest had been adequately drained for two and a half years, and there was no question of any fluid being present. Accordingly, the anaesthetist passed an ordinary endotracheal tube and allowed the patient to breathe spontaneously. The surgeon plugged the air leak at an early stage, and there was no difficulty at any time.

A variety of situations may be encountered in the case of traumatic fistulae. A tear of the main bronchus can be excluded by intubating the opposite side as indicated above; the tear may extend into the trachea, but this is of no consequence as long as the tube is airtight. After repair of the bronchus, the surgeon will usually wish to test for leaks and see whether the lung on the affected side is inflatable, and to allow this the tube can be withdrawn into the trachea. If a Carlens tube has been passed, it is merely necessary to connect up the affected side to the apparatus and inflate.

Case 7. This patient was investigated for dysphagia, and found to have a large round shadow in the right upper mediastinum. Bronchoscopy was normal, radio-active iodine studies were normal, and a test with 1 mg of tubocurarine showed no sensitivity suggestive of thymic tumour. At thoracotomy a bronchial cyst was found, adherent to the superior vena cava and the right side of the trachea, and during the dissection a hole was made in the trachea. Air leakage made adequate ventilation difficult until the hole had been sutured.

Postoperatively, the patient developed an air leak, with surgical emphysema, and at midnight on the second postoperative day it was decided to re-explore the operation site. A Carlens tube was passed under thiopentone-tubocurarine anaesthesia, and the left lung was inflated with nitrous oxide and oxygen. A good deal of muco-pus was aspirated from the right side when the patient was turned into the lateral position,

TABLE II

Type of fistula	Method	Reliability	Technical points: Difficulty	Technical points: Aspiration of pus	Technical points: Testi lea
All kinds	Antidrainage position.	Good.	Easy.	Unnecessary.	Poss
	Spontaneous respiration.	Good.	Vitiation of gases; coughing.	Possible.	Possi
	Positive pressure.	Fair.	Needs absolutely undivided attention to bag.	Possible.	Possi
Tracheal	Endotracheal tube with cuff inflated to occlude fistula.	Good; depends on position of fistula.	Usually easy.	Not possible.	Possi defl
Main bronchus (either)	Blocker in main bronchus.	Good.	Requires bronchoscopy.	Possible.	Ballo de
	Packing main bronchus.	Good.	Requires bronchoscopy and some skill.	Not possible.	Not
Right main bronchus.	Intubate left main bronchus blind: Carlens.	Fair.	May be difficult.	Possible.	Possi
	Intubate left main bronchus blind: M-L tube	Fair.	Usually easy.	Separate catheter needed.	Poss is
	Intubate left main bronchus blind: Endotracheal tube	Poor.	May be difficult.	Separate catheter needed.	Poss is
Left main bronchus	Magill endobronchial tube.	Good.	Requires bronchoscopy.		
	Intubate right main bronchus blind with endotracheal tube.	Good.	Usually easy.	Separate catheter needed.	Poss is
Upper lobe (either)	Upper lobe blocker.	Fair.	May be very difficult.	Possible.	Defl
R.U.L.	Fenestrated tube with double cuff.	Fairly good.	Usually easy.	Not possible.	Defl cu
Lower lobe.	Blocker in lower lobe.	Good.	Requires bronchoscopy; easy.	Possible.	Defl
	Packing lower lobe.	Good.	Requires bronchoscopy and some skill.	Not possible	Not

TABLE II

chnical points		Suitability		
Aspiration of pus	Testing for leaks	In children	With distorted anatomy	For various op
Unnecessary.	Possible.	Suitable.	Suitable.	Position may m difficult.
Possible.	Possible.	Suitable.	Suitable.	May be exhau inadequate operations.
Possible.	Possible.	Suitable.	Suitable.	Will annoy s pus is presen
Not possible.	Possible by deflating cuff.	Suitable.	Suitable.	Suitable for a tion.
Possible.	Balloon can be deflated.	Not suitable.	Suitable.	Not possible a monectomy.
Not possible.	Not possible.	Suitable.	Suitable.	Not possible a monectomy.
Possible.	Possible.	Not suitable.	Not suitable.	
Separate catheter needed.	Possible if tube is withdrawn.		Not suitable.	Suitable for a tion.
		Suitable.	Not suitable	
		Not suitable.	Suitable.	Suitable for a tion.
Separate catheter needed.	Possible if tube is withdrawn.	Usually suitable.	Not suitable.	Suitable for a tion.
Possible.	Deflate balloon	Not suitable.	Place under vision.	After upper l only Halton possible.
Not possible.	Deflate distal cuff.	May be suitable.	Not suitable.	Suitable for a tion.
Possible.	Deflate balloon.	Not suitable.	Suitable.	Usually not pos lower lobecto
Not possible	Not possible.	Often suitable.	Suitable.	out occludin lobe.

For various operations	Dangers
Position may make access difficult.	Air leakage.
May be exhausting and inadequate for long operations.	Spill over through unguarded fistula.
Will annoy surgeon if pus is present.	Air leak may be too gross to manage.
Suitable for any operation.	Cuff may not accurately close the fistula.
Not possible after pneumonectomy.	May be dislodged and cause spill over and/or obstruction. Upper lobe may be blocked, esp. R.
Not possible after pneumonectomy.	Pack must be very efficient to prevent spill over.
Suitable for any operation.	Flooding due to inaccurate placing, especially if tube enters right side.
Suitable for any operation.	May be dislodged or upper lobe occluded.
Suitable for any operation.	May block right upper lobe.
After upper lobectomy, only Halton blocker possible.	Obstruction, spill over and air leak from inaccurate placing or dislodgement.
Suitable for any operation.	Dangers of inaccurate placing.
Usually not possible after lower lobectomy without occluding upper lobe.	Upper lobe or middle lobe may be flooded if blocker or pack is too high.

facing page 224

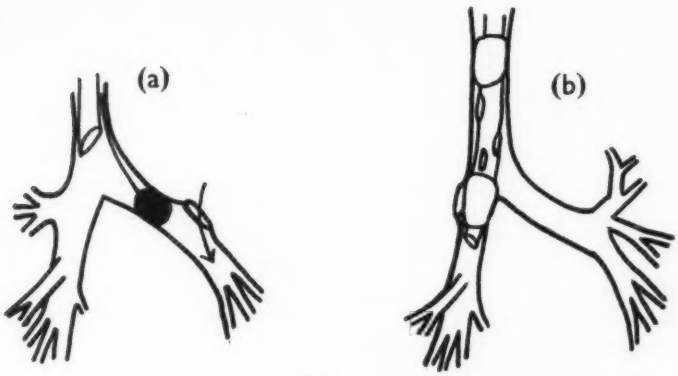

FIG. 4

Upper Lobe Fistulae

(*a*) A blocker placed above the upper lobe opening has the same functional result as intubation of the opposite side. In either case the lower lobe is left wide open to the fistula. Accurate placing of the blocker so that it completely occludes an upper lobe fistula is so uncertain and difficult that it should not be relied on, except by an expert (Halton's upper lobe blocker was designed for this purpose). If an attempt is made to pack the fistula with ribbon gauze, the lower lobe bronchus will inevitably be blocked as well, but in a really difficult case this is a small price to to pay for the prevention of flooding.

(*b*) On the right side it is much easier to place a balloon or cuff opposite the upper lobe opening with accuracy. The drawing illustrates the use of a fenestrated endotracheal tube with two cuffs.

and thoracotomy revealed a hole 2×2 mm in the trachea. It was possible to close this defect with stainless steel wire sutures and wire mesh, and the surgeon then wished to test the airtightness of the trachea. As a suitable Y-connection was not to be found at this time of night, the anaesthetist attached each bronchial tube to a separate Waters circuit, and maintained independent inflation of the two lungs. The trachea proved to be airtight, and recovery was uneventful.

It sometimes happens that the surgeon produces an unmanageably large fistula during a lung operation before the vessels are dissected, or while bleeding is going on. In addition to the anaesthetist's worries, the surgeon is irritated by the blowing of sputum into the operative field, and a certain mutual lack of sympathy quickly becomes apparent. Under these circumstances, the most satisfactory answer is for the surgeon to put a Crafoord clamp across the whole hilum. This effects a functional pneumonectomy for the anaesthetist, and gives the surgeon a clean dry field with an immobile lung.

ANAESTHETIC MANAGEMENT

As far as nonthoracic operations for unassociated conditions are concerned, only comparatively fit patients with long standing fistulae are likely to be presented, and they should give little trouble. Spontaneous respiration should be preserved wherever possible, and there is a place here for local and regional methods. The only other type of case which may give rise to difficulty is the spontaneous pneumothorax or the artificial pneumothorax who turns out, when inflated, to have a fistula. As long as the possibility of a tension pneumothorax is remembered, and treatment is not delayed, all will be well.

In the case of chest operations directly related to the lesion, the first choice to be made is between local and general anaesthesia. Many small procedures, such as rib resection, can be performed under local, but there are circumstances which often make general anaesthesia desirable:

the condition of the patient, sepsis in the operation area, doubt as to the diagnosis and extent of the operation, long and major procedures, nervousness of the patient, and childhood may be given as examples. In these cases there is a second choice to be made in selecting one of the possible general anaesthetic techniques. Many of the specific indications for particular methods of anaesthesia have already been discussed in relation to the characteristic problems involved, and it is hardly possible to say more about this without expressing merely individual preferences. The number of bronchial fistulae coming to surgery is quite small, and no one anaesthetist sees enough cases to be dogmatic about their management. Furthermore, in this condition it may safely be assumed that in some respect each case will be quite different from all the rest. The main purpose of this paper is to indicate the basic principles involved in the handling of fistulae; if these principles are applied to the individual case it will be found that the possible methods of approach are reduced to, at most, two or three, and the final choice will usually be determined by the anaesthetist's personal experience with the various techniques (table II).

Although some cases present a clear cut picture with a definite pre-operative diagnosis, it is not uncommon to be confronted with a rather doubtful case, in which the presence, or the size, of a fistula is uncertain. The intended operation may be short, and there may be no clear indication for a special technique; the surgeon himself may wish to find out whether there is a fistula, or where it is blowing from, in order to effect a repair, and in either of these cases the use of a blocker is inconvenient to him. For cases of this kind, the following "safety first" method is suggested.

A dextrose drip is set up with a threeway tap, as a convenient route for injections, and in case blood transfusion is needed. Any drainage tube in the chest is unclamped, and the patient is preoxygenated for at least three minutes in a semi-sitting position. He is then given a sleep dose of thiopentone, and a small dose, about 25 mg, of suxamethonium, and allowed to continue breathing oxygen until respiration ceases. His larynx and trachea are then sprayed with 4 per cent lignocaine through a Macintosh spray, and he is intubated with a cuffed tube. The cuff is inflated and the patient is connected to a Waters bag and given nitrous oxide and oxygen. The lungs are then gently inflated, and if the apparatus is leakproof, the size of the fistula can be estimated. If, as is usually the case, it is a small leak, a canister is included in the circuit, and controlled respiration is continued with intermittent doses of suxamethonium. If the fistula is gross, or if at any stage during the operation the surgeon makes it so, the patient can be left to breathe spontaneously and given a little trichloroethylene if necessary. All this induction is carried out in the semisitting position, so that the anaesthetist has the opportunity of dealing with his problems one by one, and can make a fair appraisal of the air leakage difficulty before he gets into any trouble with the other difficulty, spillover of secretions. Once the induction is completed, the positioning of the patient is governed by his X-ray and the surgeon's requirements, but throughout the procedure the suction machine stands by the anaesthetist's side, switched on, and with catheter ready attached, so that instantaneous action can be taken if there is any sign of contamination of the airway during the changes of posture.

Finally there remains to be considered the anaesthetic management of chest injuries. Any major injury to the chest, open or closed, may be complicated by air leakage, either from lacerated pulmonary tissue or from a major bronchus. With an uncontrolled open pneumothorax, one of the most important factors contributing to the poor state of the patient is the presence of paradoxical breathing and mediastinal flap; the same applies to closed crush injuries with multiple fractured ribs, in which the stability of the chest wall is lost. Coughing is ineffective, and in the presence of a fistula, blood from the site of injury may be disseminated throughout the bronchial tree. In these cases controlled respiration is of enormous benefit: paradox and mediastinal flap are abolished, and the improvement in the patient's condition, often accompanied by a return to consciousness as carbon dioxide is washed out, is dramatic. As soon as is practicable, the bronchial tree should be thoroughly sucked out through a bronchoscope, and there is something

to be said for using a short acting relaxant to institute controlled respiration, in case it proves impossible to keep up with the airleak. The danger of tension pneumothorax may be guarded against, in a closed case, by putting a needle into one of the upper intercostal spaces anteriorly, and leaving it there.

The use of relaxants can make a great difference to the prognosis of these cases, and in the event of future hostilities, in which large numbers of chest injuries may occur, some provision for organized management would be well worth while.

ACKNOWLEDGMENTS

By no means all the cases quoted were personally anaesthetized by the author. I should like to express thanks to the surgeons of the Liverpool Thoracic Surgical Unit, and to doctors G. Jackson Rees, E. S. N. Fenton, J. C. Richardson and J. E. Riding, for help and permission to publish.

REFERENCES

Barrett, N. R. (1950). *Techniques in British Surgery*, p. 157. Philadelphia: Saunders.

Belcher, J. R., and Grant, I. W. B. (1955). *Thoracic Surgical Management*, 2nd ed., p. 108. London: Baillière, Tindall and Cox.

Brock, R. C. (1952). *Lung Abscess*, p. 166. Oxford: Blackwell.

Coope, R. (1951). *Diseases of the Chest*, 2nd ed., p. 430. Edinburgh: Livingstone.

Coryllos, P. N. (1937). A new conception of tuberculosis empyemata based on their pathologic physiology. *J. Thorac. Surg.*, **7**, 48.

Crafoord, C. (1938). On the technique of pneumonectomy in man. *Acta chir. scand.*, **81**, 1.

Dundee, J. W. (1955). Tension Pneumothorax and the induction of Anaesthesia. *Anaesthesia*, **10**, 74.

Gale, J. W., and Waters, R. M. (1932). Closed endotracheal anaesthesia in thoracic surgery. *J. thorac. Surg.*, **1**, 432.

Gray, T. C., and Edwards, F. R. (1948). The Anaesthetic problems associated with giant tension cysts of the lung. *Thorax*, **3**, 237.

Halton, J. (1943). A method of controlling Bronchial Secretion in Thoracic surgery. *Lancet*, **1**, 12.

Hewer, C. L. (1944). *Recent Advances in Anaesthesia and Analgesia*, 5th ed., p. 123. London: Churchill.

Huizinga, E., and Smelt, G. J. (1950). *Bronchography*, p. 203. Assen: van Gorcum.

Lee, J. A. (1953). *Synopsis of Anaesthesia*, 3rd ed., p. 406. Bristol: Wright.

Macintosh, R. R., and Leatherdale, R. A. L. (1955). Bronchus Tube and Bronchus Blocker. *Brit. J. Anaesth.*, **27**, 556.

Magill, I. W. (1936). Anaesthetics in Thoracic Surgery with special reference to Lobectomy. *Proc. roy. Soc. Med.*, **29**, 643.

Mansfield, R. (1947), quoted by Organe, G. (1949), p. 455.

Mülly, K. (1950). Uber die Bedeutung der Intubationsnarkose in der Lungenchirurgie. *Schweiz. Z. Tuberk.*, Suppl. Biblio. Tuberc., Fasc. 4.

Mushin, W. W., and Rendell-Baker, L. (1953). *The Principles of Thoracic Anaesthesia*, p. 19. Oxford: Blackwell.

Nosworthy, M. D. (1941). Anaesthesia in Chest Surgery with Special Reference to Controlled Respiration and Cyclopropane. *Proc. roy. Soc. Med.*, **34**, 479.

Organe, G. (1949). *Modern Practice in Anaesthesia*, 1st. ed., p. 459. London: Butterworth.

Schweizer, U., and Howland, W. S. (1956). The diagnosis and treatment of tension pneumothorax complicating radical surgery about the head and the thorax. *Anaesth. et Analg.*, **35**, 375.

Vellacott, W. H. (1954). A New Endobronchial Tube for Bronchopleural Fistula Repair. *Brit. J. Anaesth.*, **26**, 442.

XI CONGRESSO SOCIETA ITALIANA ANESTESIOLOGIA

SYMPOSIUM ON CURARE AND OTHER MUSCLE RELAXANT DRUGS

A Symposium dealing with curare and other muscle relaxant drugs will be held in September 1958, under the auspices of the Ospedale al Mare, Venice.

There will be discussions on the Chemical, Pharmacological, Physical and Clinical aspects of muscle relaxants. The meeting will be held in connexion with the 11th Congresso Societa Italiana Anestesiologia and enquiries should be made to the Organizing Committee, c/o Dr. Ruggero Rizzi, Ospedale al Mare, Venice, (Lido), Italy.

Brit. J. Anaesth. (1957), **29**, 228

DOSES OF CURARE

A Plea for their Reduction

BY

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THE major development in anaesthesia during the last decade has been " to give light general anaesthesia to ensure unconsciousness, and then to abolish reflex response to stimuli by one of the relaxants which in themselves do not cause any metabolic upset " (Macintosh, 1955). While many anaesthetists are trying to reduce the analgesic and hypnotic agents to a minimum, relaxants are being given with little restraint because they are assumed to be innocuous. Often curarization is used to cover up poor anaesthesia (Cullen, 1954). In Britain doses of d-tubocurarine (dtc) are large. With or without a test dose (Gray and Halton, 1948) the initial dose frequently reaches 30 mg or more. For instance, Grigor (1954) used 35 mg for intubation in a case of mitral stenosis. Collier (1956) injects 25–30 mg for intubation for Caesarean section, and Lawson (1956a) gave 120 mg gallamine for intubation to a man of 73 whose abdominal muscles were already relaxed by spinal analgesia.

In view of several reports of death after heavy curarization, and of the assumption that there occur more anaesthetic deaths in curarized than in noncurarized patients (Beecher and Todd, 1954) the time may have come to reconsider the dosage of curarizing agents. This paper is a plea for individualizing the doses of the nondepolarizing relaxants and for moderation in their use.

Lately, fatalities after large doses of dtc have been reported in this journal (Foster, 1956) which were thought to be caused by potassium depletion and not by an overdose of relaxant. One of these cases is quoted in full in order to show how its problems could be seen in a different light:

A man of 78 years was treated for 8 days in a medical ward for chronic intestinal obstruction caused by a carcinoma of the pelvirectal junction. This was precipitated into an acute obstruction by the use of barium in X-ray studies. He became grossly distended and vomited considerable amounts of fluid which were inadequately replaced with saline and dextrose.

He was presented for emergency surgery dehydrated, and with electrolyte depletion—serum Na 130.5 m.equiv/l., K 3.2 m.equiv/l., Cl 82.4 m.equiv/l. His blood urea had recently risen to 115 mg per cent.

Premedication was with atropine 0.6 mg and morphine 10 mg.

The patient was given oxygen to breathe for several minutes and then nitrous oxide and oxygen (6 l./min and 2 l./min respectively). Simultaneously an intravenous test dose of 5 mg dtc was given. This did not evoke an abnormal depression of breathing, so that a further 25 mg was given as consciousness was lost, and the patient intubated. He was so restless—moving his arms and legs, shaking his head, opening his eyes, and breathing—that within 10 minutes a further 10 mg of dtc was given. This had little immediate effect, but after about 10 minutes again he suddenly became quiet, remaining thus throughout the operation. Towards the end a further dose of 10 mg dtc was given during closure of the very distended abdomen. This total dose of 50 mg dtc spread over 1½ hours operating time is not considered unusual for the technique employed.

Faint respiratory movements were present at the end of operation, so atropine 1.2 mg was given intravenously, followed by neostigmine 5 mg for reversal of curarization. The effect was barely perceptible. A further dose of 2.5 mg neostigmine was given after 15 minutes, and this dose was repeated at hourly intervals. In the meantime, other resuscitative measures were tried, including nalorphine, bemegride (Megimide), nikethamide, alterations in inspired carbon dioxide tension, inflation with pure oxygen, intravenous potassium infusion, and intravenous noradrenaline infusion when it was found that his blood pressure had fallen to about 65 mm Hg systolic. (On admission his blood pressure had been 200/100 mm Hg.) None of these measures produced more than a mild transient response, bemegride being the most effective. After the last dose of neostigmine, when 15 mg had been given altogether over 3 hours, res-

piration virtually ceased. Despite prolonged ventilation with oxygen, his unconsciousness persisted, together with inadequate respiration and hypotension that responded but poorly to noradrenaline infusion. He died about 14 hours after the operation.

From the description of the induction two facts stand out:

(1) d-Tubocurarine did not act in a way one would expect.

(2) The patient was not asleep—as opening of eyes, moving of limbs and shaking of the head are as much signs of being awake as of potassium loss.

The delayed action of dtc—it did act after 20 minutes—may be explained by lack of potassium, or by dehydration, or by metabolic changes or by some toxin (Stewart, 1956) just as the duration of the dtc effect in these cases is prolonged (Morkane and Pryor, 1956). Whatever the reason, it has no bearing on the need for revision of technique. A patient who retains voluntary movements under an appropriate mixture of nitrous oxide and oxygen ought to be *anaesthetized*, not relaxed. In a case of deranged metabolism this is best done by any of the gaseous agents, as they pass through the body unchanged, be it cyclopropane, be it "minimal" ether. If after light surgical anaesthesia had been established, dtc had not acted, one might have considered trying a different relaxant; e.g. 20 mg gallamine can, in my experience, change an incomplete dtc relaxation into a very satisfactory one; or one might have had to deepen general anaesthesia. But little can ever be gained by pushing a drug which does not seem to act in a given individual in the average way. An initial dose of 30 mg dtc appears to be unduly large for an old, seriously ill patient who could most likely have been intubated with ease on 12–15 mg. To this relative overdose a further 20 mg were added within an hour. On the other hand, for maintenance he received only nitrous oxide which offers poor protection of the central nervous system against stimuli which an operation on an irritated peritoneum elicits.

Since Pick and Unna's (1945) work it has been known that large doses of dtc cause central depression in frogs. In the cited case a central effect manifested itself by depressed respiration and circulation, and by persistent unconsciousness which should have passed quickly once nitrous oxide was discontinued. The depression may have been simply due to overdose—50 mg dtc for an aged, dehydrated, toxic and uraemic patient—or, as Foster suggests, to an alteration in the selectiveness of the blood brain barrier which might have enhanced the effect of this large dose. In any case, one cannot help wondering whether the same course of events would have followed if an aggregate 20–25 mg dtc had been given and fewer painful stimuli had reached the brain.

The anaesthetic technique for closure of the abdomen does not appear quite logical as dtc was tried again though a delayed action ought to have been expected after the initial experience. There seems to have been the choice between two possibilities: either relaxation had worn off, then a different relaxant might have been tried, or—a frequent occurrence in cases of ileus which receive ample doses of relaxant at the beginning—the abdominal muscles were still well relaxed but the distended bowel could not be returned into the abdomen. As relaxants cannot reduce distension of the gut other measures have to be applied by the surgeon: a needle or a rubber tube is inserted into the bowel through the centre of a field surrounded by a purse string suture and the gases or fluid are removed by suction. In addition, the anaesthetist can break the operating table in such a way that head and feet are raised and the bowel sinks back into the abdominal cavity.

Two further aspects of the technique might have had a bearing on the outcome:

(1) Blood transfusion has not been mentioned. We transfuse every case of intestinal obstruction during operation because we feel certain that it is beneficial to a seriously ill patient during a shock-producing operation, as such a laparotomy is bound to be due to handling of the gut during the search for the obstruction, or extrusion of bowel, or bowel resection. Besides most of our patients suffer from secondary anaemia; amongst our new immigrants especially we hardly ever find more than 11–13 g haemoglobin per 100 ml blood. Our slightly anaemic patients recover more quickly if part of their deficiency has been made good during operation. As a corollary, we introduce at least some blood with a normal potas-

sium content, even if an existing hypokalaemia has not been corrected before the start.

(2) An intravenous noradrenaline infusion was given when the patient's blood pressure had fallen to about 65 mm Hg systolic. In our own practice the circulation of a hypertensive patient of 200/100 mm Hg, as the cited case, receives support already when the pressure drops to about 130, usually by speeding the blood transfusion, and if this does not reverse or at least stop the fall, by the use of a vasopressor. We believe that it is much easier to stay out of trouble than to extricate oneself from serious difficulties once they have arisen. Lawson (1956b) has enumerated four factors which can lead to fatal results in such cases: too much relaxant, too much anaesthesia, too much premedication, and too little resuscitation.

It is the excellent and detailed description of the case which lays it open to criticism because it makes it easy to visualize the course of events. There are sure to be many more cases managed by similar technique. For instance, Hunter (1956) collected six cases where after tubocurarine or gallamine respiration did not return, neostigmine did not have any effect and the patients died. He states that in every case the patient was elderly and in poor condition, but that the relaxant dose was " not excessive ". Scott and Clarke (1956) gave to a " small wizened lady of 67, weighing 6½ stone " 80 mg of gallamine, a dose which will produce temporary apnoea in many a muscular man. These examples could probably be multiplied if one analyzed the doses of curare given to those " neostigmine-resistant " patients whose deaths have been reported in the wake of Dr. Hunter's paper.

To illustrate my plea for individualized doses I report briefly on four cases whose general anaesthesia was maintained by different techniques:

CASE 1

A.B., 61 years old, male. Small bowel ileus.

Operation. Laparotomy revealed patchy gangrene of large parts of small bowel; extensive resection.

Anaesthesia time. 1 hour 50 min.

General condition. Good physical habitus, but very ill.

Premedication. Morphine 10 mg and atropine 0.5 mg.

Induction. 250 mg 2.5 per cent thiopentone, 60 mg suxamethonium, spraying of the cords with a cocaine-amethocaine mixture after inflation with oxygen, intubation, followed by further 250 mg thiopentone.

Maintenance. Nitrous oxide-oxygen with traces of ether, a further 350 mg thiopentone given in 3 doses, and 100 mg pethidine (50 mg + 25 mg + 25 mg). 12 mg dtc after skin incision, 40 mg gallamine after opening of peritoneum. 40 mg gallamine before closure of peritoneum. Sufficient respiratory excursions at the end of operation. Received 800 ml citrated blood before and during operation.

Satisfactory recovery during the first 3 days but renewed ileus after 5 days when on reopening the abdomen almost the whole bowel was found to be gangrenous. Died shortly afterwards.

CASE 2

A.F., 63 years old, male. Carcinoma ventriculi.

Operation. Subtotal gastrectomy.

Anaesthesia time. 4 hours.

General condition. Fair. Blood pressure 195/95 mm Hg. Emphysematous thorax, severe kyphoscoliosis. Hb 8.8 grams per cent after transfusion.

Premedication. 50 mg pethidine and 0.5 mg atropine.

Induction. 500 mg 2.5 per cent thiopentone in 3 doses, 50 mg suxamethonium, inflation, spray, intubation.

Maintenance. Nitrous oxide-oxygen and " minimal ether " (35 ml in Heidbrink machine). Before opening of the peritoneum 15 mg dtc, requiring controlled respiration for one hour, then aided ventilation. No further dtc required. Once 50 mg thiopentone were needed when an attempt to continue without ether failed. Towards closure of peritoneum 50 mg thiopentone, for closure 20 mg gallamine. Awake on table with satisfactory spontaneous respiration. Received 1,200 ml citrated blood during operation. Uneventful recovery.

CASE 3

H.K., 80 (or more) years old, female. Incarcerated para-umbilical hernia.

Operation. Herniotomy and hernioplasty of para-umbilical and umbilical herniae.

Anaesthesia time. 1 hour 20 min.

General condition. Poor. Dehydrated. Single râles over lungs.

Premedication. 0.25 mg scopolamine.

Induction. 400 mg 2.5 per cent thiopentone in 2 doses, 20 mg suxamethonium, inflation, spray, intubation.

Maintenance. Nitrous oxide-oxygen and trichloroethylene; controlled ventilation by means of Salt valve. 5 mg dtc after skin incision, a further 6 mg 5 minutes later. Another 4 mg required after 40 minutes. Awake on table with sufficient respiratory excursions. Received 400 ml citrated blood during operation. Uneventful recovery.

CASE 4

R.S., 70 years old, female. Severe obstructive jaundice. ?Tumour.

Operation. Exploration, carcinoma of pancreas found, choledocho-jejunostomy.

Anaesthesia time. 2 hours 15 minutes.

General condition. Poor, blood sugar 205 mg per cent, no sugar in urine. Hb 10.8 g per cent.

Premedication. 0.5 mg atropine.

Induction. 200 mg 2.5 per cent thiopentone in 2 doses which sufficed for intubation after spray, though there was a little bucking on the tube.

Maintenance with intermittent cyclopropane and nitrous-oxide; 6 mg dtc after skin incision, 3 mg before opening of the peritoneum. Aided ventilation. Additional 3 mg required after further 40 minutes, 20 mg gallamine for closure of peritoneum. Awake with last skin suture, sufficient respiratory excursions. Received 400 ml citrated blood during operation. Uneventful recovery.

The following principles are followed in this type of anaesthesia. After any suitable induction intubation is performed under suxamethonium unless prolonged apnoea is feared, as in case 4. Light anaesthesia is established and stabilized while the patient is placed and draped. This provides a base line from which to observe the effect of the relaxant which is injected soon after the beginning of the operation in a dose thought by experience to be appropriate for that particular patient. Before the peritoneum is reached, one can judge from the respiratory excursions or from the feel of the rebreathing bag whether this dose will suffice or whether a further injection must be added; e.g., in case 2, 15 mg dtc lasted surprisingly enough for more than 3 hours while in case 3 the initial dose had to be repeated almost immediately. In case 1 dtc did not act satisfactorily and the relaxant was changed. By thus testing the effect on the individual the required relaxation is achieved with a minimum amount of drug. Further doses during the course of the operation usually have a definite relation to the aggregate amount which was needed for the opening of the abdomen. The first repeat dose is about half that amount, later ones are smaller. For closure one can either give the last dtc injection not less than 40 minutes before the end of the operation (Hewer, 1957) or, as such accurate timing is not always possible, inject a small dose of gallamine before suture of the peritoneum. Usually sufficient spontaneous respiration has returned before the skin is closed.

Average doses. For a healthy muscular man we start with 15 mg dtc which in rare cases have to be raised to 18 or 20 mg. In an elderly or ill man 12 mg are tried. A normal female patient receives 12 mg for upper abdominal surgery, 9 mg for gynaecological operations. These doses would also suffice in most cases for intubation if one wanted to avoid suxamethonium. If much distension is expected, or if the patient is either hefty or old, or in poor condition, the amounts are increased or decreased respectively.

This dosage of relaxants is neither original nor new. In fact, it approaches the amounts advocated by Gray and Halton (1946) in their original publication, where they stated that 20 mg dtc were sufficient to relax the average healthy abdomen, that intermittent doses of 2–4 mg were added after induction with a barbiturate and 15 mg dtc, and that in the aged an initial dose of 10 mg was suitable.

There are exceptions to these averages. Firstly, those patients in whom any possible reaction to laryngoscopy and intubation has to be avoided, i.e., cases of raised intracranial pressure or gross circulatory disturbances. Luckily they are not the ones in whom a persistent suxamethonium apnoea may be expected. Therefore the suxamethonium dose can be ample, 70 mg for a female, up to 100 mg for a man. Secondly, the patient whose distended abdomen is closed by through-and-through sutures and where, therefore, complete relaxation has to be procured up to the very end of the operation. Thirdly, the case where exploratory laparotomy reveals an inoperable condition and closure has been completed before the effect of the relaxant has worn off. In the latter two instances one might be justified in using neostigmine.

If the patient is very ill and it is difficult to judge whether closure of the abdomen can be effected without adding more relaxant, we request the surgeon to try whether he can close the peritoneum easily. If not, we ask him to wait for the effect of a further small injection of relaxant. In these cases we deliberately do not anticipate the surgeon's requirements but prefer a slightly impatient surgeon to a depressed or apnoeic patient. Most surgeons will readily agree to a delay of two or three minutes, once they realize that this adds to the patient's safety.

For the main part of the operation our choice is generally dtc because with a rise of pulse rate and blood pressure after gallamine it is sometimes difficult to determine whether it is due to

the drug or to other causes. But once a patient's pulse rate and blood pressure have remained steady through most of the operation, a rise after gallamine for closure is no reason for concern, as its cause is not in doubt. It is my clinical impression that gallamine given in equipotent doses of dtc gives the more complete relaxation. Apart from this profound flaccidity, gallamine for closure has the advantage that a small dose in combination with any dtc which remains in the body will go far, and that its effect passes off quickly. Gallamine alone is used when bronchospasm is feared or when a short operation is anticipated.

These are personal preferences which will vary with the anaesthetist. But whether one likes to use dtc alone, or gallamine alone, or both combined, a technique can usually be found of dosing and timing which will leave the patient at the end of the operation with sufficient spontaneous respiration to make the use of antidotes superfluous. Neostigmine has a mortality of its own. Since Macintosh (1949) drew our attention to it, many cases have been reported, e.g., 5 cases have been collected lately (Edwards et al., 1956). It ought not to be used routinely but only when specially indicated. Hewer (1957) rightly considers the use of an antagonist a confession of failure. If at the end of an operation respiratory depression has partially passed off it is safer to continue with aided ventilation until satisfactory respiratory excursions are restored. If after some trial sufficient respiratory exchange does not return, neostigmine can be injected 5–10 minutes after 0.5 mg atropine, starting with 1 mg (Doughty and Wylie, 1952) with increments of 0.5 mg until the desired effect is obtained. While hardly a day passes without my injecting dtc and/or gallamine to several patients, the need for neostigmine arises three or four times a year.

During the lively discussion which followed Hunter's (1956) paper on neostigmine-resistant curarization it has been suggested that the combination of suxamethonium followed by one of the competitive relaxants may have led to persistent apnoea which neostigmine could not reverse (Gordon, 1956; Verrill, 1956; Beardsworth, 1956). Using this combination as a standard technique for at least three years we have never experienced such an event. This strengthens our conviction that the doses and not the drugs are the cause of such incidents.

Doses of curare are not the same everywhere. Our American colleagues seem to get satisfactory results with much smaller amounts, just as their thiopentone doses are about half those used in Britain (Dundee, Price and Dripps, 1956). For instance, Patterson (1952) advocates 3–9 mg dtc, thiopentone and an analgesic spray for intubation, and maintains relaxation by repeated injections of fractional doses of one of the relaxants. Sadove et al. (1955) use 6–8 mg dtc for intubation of patients due to undergo mitral commissurotomy. They take special care that bucking does not occur. There seems to be too wide a gap between this dose and the 35 mg of Grigor (1954) for the same kind of case.

Nosworthy stated in 1953 that "by an accurately judged dose of relaxants—or by a series of graded injections—it should not be too difficult to produce just about that degree of peripheral suppression which one has learned is required for any given procedure". His sound advice ought not to be forgotten. The relaxants have enabled us to carry the old, the frail, and the very ill safely through long hours of difficult surgery. It would be a great pity if one of the greatest boons in anaesthesia were discredited through injudicious use and overdose. We all have learned to work satisfactorily with "minimal ether" i.e. with amounts which just suffice to produce a required result. It might reduce anaesthetic fatalities if we trained ourselves, too, to use "minimal curare".

SUMMARY

While anaesthetists try to reduce the use of analgesic and hypnotic agents to a minimum, relaxants are given in large doses as they are thought to be innocuous. As several deaths have been reported after heavy curarization, though they are ascribed to other causes, it is suggested that the dosage should be modified.

One fatal case reported in the literature is analyzed in detail. The author's technique of achieving the required relaxation with a minimal amount of nondepolarizing relaxants is illustrated by case reports.

It is suggested that by correct dosing and

timing of relaxants the use of antagonists should be avoided.

A plea is made for the use of "minimal curare".

REFERENCES

Beardsworth, B. S. (1956). Neostigmine-resistant Curarization. *Brit. med. J.*, **2**, 1055.

Beecher, H. K., and Todd, D. P. (1954). Deaths associated with Anaesthesia and Surgery. *Ann. Surg.*, **140**, 2.

Collier, H. (1956). Caesarean Section: A Method of Anaesthesia. *Brit. J. Anaesth.*, **28**, 130.

Cullen, S. C. (1954). *Anesthesia in General Practice*, 4th ed., p. 140, Chicago: The Year Book Publishers Inc.

Doughty, A. G., and Wylie, W. D. (1952). Antidotes to "True" Curarizing Agents. *Brit. J. Anaesth.*, **24**, 66.

Dundee, J. W., Price, H. L., and Dripps, R. D. (1956). Acute Tolerance to Thiopentone in Man. *Brit. J. Anaesth.*, **28**, 344.

Edwards, G., Morton, H. I. V., Pask, E. A., and Wylie, W. D. (1956). Deaths associated with Anaesthesia. *Anaesthesia*, **11**, 194.

Foster, A. P. (1956). Potassium Depletion and the Central Action of Curare. *Brit. J. Anaesth.*, **28**, 488.

Gordon, J. (1956). Neostigmine-resistant Curarization. *Brit. med. J.*, **2**, 1054.

Gray, T. C., and Halton, J. (1946). A Milestone in Anaesthesia? (d-Tubocurarine Chloride). *Proc. roy. Soc. Med.*, **39**, 400.

—— —— (1948). Idiosyncrasy to d-Tubocurarine Chloride. *Brit. med. J.*, **1**, 784.

Grigor, K. C. (1954). Atelectasis during Anaesthesia. *Anaesthesia*, **9**, 185.

Hewer, C. L. (1957). Neostigmine-resistant Curarization. *Brit. med. J.*, **1**, 45.

Hunter, R. A. (1956). Neostigmine-resistant Curarization. *Brit. med. J.*, **2**, 919.

Lawson, J. I. (1956a). Cardiac Arrest following the Administration of Neostigmine. *Brit. J. Anaesth.*, **28**, 336.

Lawson, J. I. M. (1956b). Neostigmine-resistant Curarization. *Brit. med. J.*, **2**, 1544.

Macintosh, R. R. (1949). Death following Injection of Neostigmine. *Brit. med. J.*, **1**, 852.

—— (1955). A Plea for Simplicity. *Brit. med. J.*, **2**, 1054.

Morkane, C. J. J., and Pryor, W. J. (1956). Anaesthesia for Intestinal Obstruction. *Anaesthesia*, **11**, 245.

Nosworthy, M. D. (1953). A Return to Simplicity? *Anaesthesia*, **8**, 247.

Patterson, R. L. (1952). The Use of Muscle Relaxing Drugs in Anesthesia. *Curr. Res. Anesth.*, **31**, 65.

Pick, E. P., and Unna, K. (1945). The Effect of Curare and Curare-like Substances on the Central Nervous System. *J. Pharmacol.*, **83**, 59.

Sadove, M. S., Wyant, G. M., Julian, O. C., and Dye, W. S. (1955). Anesthesia for Mitral Commissurotomy. *Anesthesiology*, **16**, 133.

Scott, W. E. B., and Clarke, J. C. (1956). Neostigmine-resistant Curarization. *Brit. med. J.*, **2**, 1174.

Stewart, K. A. (1956). Neostigmine-resistant Curarization. *Brit. med. J.*, **2**, 1174.

Verrill, P. J. (1956). Neostigmine-Resistant Curarization. *Brit. med. J.*, **2**, 1054.

ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

JUBILEE MEETING

The Association of Anaesthetists of Great Britain and Ireland is celebrating the twenty-fifth anniversary of its formation this year, and is holding its Annual Meeting on December 4, 5, 6 and 7, 1957, at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2.

The provisional programme is as follows:

Wednesday, December 4
Evening: The Association will hold a Cocktail Party to welcome those overseas visitors who will attend the meeting.

Thursday, December 5
Morning session: Papers.
Afternoon session: Annual General Meeting. Frederic Hewitt Lecture.
Evening: Annual Dinner.

Friday, December 6
Morning session: Papers.
Afternoon session: Papers. Meeting of the Section of Anaesthetics of the Royal Society of Medicine.
Evening: Cocktail Party given by the Faculty of Anaesthetists. Dance.

Saturday, December 7
Morning session: Symposium.

Throughout the Meeting there will be a Scientific Exhibition and a Trade Exhibition.

The final date for submission of papers for presentation at this meeting is June 1, 1957.

Further particulars will be available later on application to the Secretary, Association of Anaesthetists of Great Britain and Ireland, 45 Lincoln's Inn Fields, London, W.C.2.

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A SIMPLE PAEDIATRIC TRANSFUSION APPARATUS

BY

MARK MEHTA

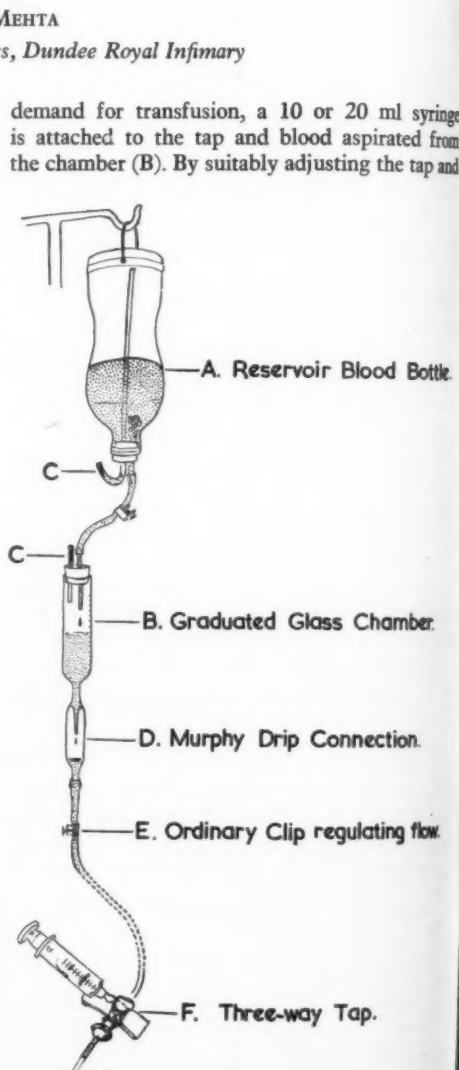
Department of Anaesthetics, Dundee Royal Infirmary

DURING operations on infants and children, timely and adequate replacement of lost fluid is essential. Moreover, the fluid and electrolyte balance is so easily disturbed that it is important to measure the replacement fluid accurately (LeQuesne, 1954). Gross (1953) used a burette type of transfusion set. This would appear to be unnecessarily complicated, requiring the use of a special syringe. There is, also, no protection of the transfused fluid from airborne infection. To overcome these defects the following apparatus has been assembled from standard materials.

Description of Apparatus and Method of Use.

The diagram shows the general plan of the transfusion apparatus. Blood or other fluid, from the reservoir bottle (A), can be run in, as required, into a 50 ml chamber (B), with 5-ml divisions. The measuring jar illustrated here is commonly used for gastric milk feeding, but this was graduated and adapted for use in this connection by fusing the lower end to a Murphy drip (D). The rate of flow is adjusted by clip (E). To prevent contamination from the outside atmosphere glass wool was inserted into the air inlet tubes (C). P.V.C. (polyvinyl chloride) tubing has been used instead of rubber because it withstands autoclaving and storage without cracking or becoming tacky. This transparent material shows up air emboli or any foreign particles, due to faulty cleaning. Moreover, thrombophlebitis is less common with plastic than rubber connecting tubing (Jones, 1954; Medical Research Council, 1957).

Gravity alone cannot maintain a rapid rate of transfusion through the narrow channels available. A three-way tap (F) not only provides an efficient means of rapidly increasing the flow, but also enables the easy administration of drugs for anaesthesia or resuscitation. When there is an urgent demand for transfusion, a 10 or 20 ml syringe is attached to the tap and blood aspirated from the chamber (B). By suitably adjusting the tap and



exerting some force on the plunger of the syringe, the fluid can be rapidly introduced into the blood stream. There is no leakage at the unions or filling up of the Murphy drip chamber, as may occur with a transfusion pump or Higginson syringe.

"Portex" nylon tubing of adequate diameter allows a free flow of blood and is used for connecting the three-way tap to the vein. This material can be sterilized by boiling or steam heat up to 160°C, but not by dry heat, which makes it too brittle.

This tubing is put into the saphenous vein, at the ankle or in the groin, before operation. It is then gently pushed along the vein until it is judged to be within one of the larger channels. By this means the anaesthetic agent or tranfusing fluid is introduced directly into the central venous stream, where relatively larger volumes can be accommodated. Any irritant, so introduced, is consequently more rapidly diluted and irritation of the vein wall and thrombosis less likely to occur (Le Quesne, 1954).

ACKNOWLEDGMENTS

My thanks are due to Mr. J. Grieve for much help and constructive criticism; also to Dr. W. Shearer, Sister E. Young, and Miss M. Mackenzie for the diagram.

REFERENCES

Gross, R. E. (1953). *Surgery of Infancy and Childhood*. 1st ed., p. 34. London and Philadelphia: W. B. Saunders Company.

Jones, P. F. (1954). Thrombophlebitis following Intravenous Infusions. *Lancet*, **2**, 970.

Le Quesne, L. P. (1954). *Fluid Balance in Surgical Practice*, 1st ed., pp. 97, 112. London: Lloyd-Luke.

Medical Research Council (1957). Thrombophlebitis following Intravenous Infusions: Trial of Plastic and Red Rubber Giving-sets. *Lancet*, **1**, 595.

BOOK REVIEW

The First Hundred Years. Published by Pfizer Ltd. Pp. 92.

The title of this little book, by an anonymous author, gives little idea of its contents. This is clarified in the opening sentence which reminds readers that it is just over one hundred years since Thomas Addison focused attention on the clinical significance of the adrenal gland by publication of his monograph on "The Constitutional and Local Effects of Diseases of the Suprarenal Capsules." It is, in fact, devoted entirely to corticosteroid therapy and aims to present a clinical evaluation of these compounds in those conditions for which they are specifically indicated.

The opening chapter deals with the history, chemistry and physiology of the glucocorticoids, although the latter aspect is not discussed in great detail. The formidable list of clinical indications for systemic hydrocortisone in chapter 2 makes one realize that "we are now in the corticosteroid age." These opening chapters will be of greater interest to the anaesthetists than the subsequent ones dealing with dermatology and ophthalmology. Those who are, from time to time, requested to inject local anaesthetics into fibrotic nodules should benefit from reading the section on the use of hydrocortisone for this purpose.

Mention is made of the newly introduced preparations, prednisone and prednisolone, but it is rather surprising to find the latter (which is not available in an injectable preparation) recommended for pre- and postoperative substitution therapy after adrenalectomy. One notable omission is a discussion of the hazards of anaesthesia in patients undergoing glucocorticoid therapy, although the use of the latter drug in circulatory failure is mentioned.

The book concludes with a brief review of the literature on Viadril, which is the steroid of most interest to the anaesthetist.

The large type makes very easy reading and the book is well produced and for the average medical practitioner presents an easily readable review of this difficult and specialized subject.

John W. Dundee

Brit. J. Anaesth. (1957), **29**, 236

LOW RESISTANCE NASAL ENDOTRACHEAL UNIONS

BY

F. L. ROBERTSHAW

Park Hospital, Davyhulme, Manchester

THE original curved Magill endotracheal tube unions, being smooth, tend to slip out of the tube very easily. Being small they are often rather fiddling to handle in moments of haste and urgency. The alternative right angle unions of Rowbotham are easier to handle and more secure but have a higher resistance to gas flow owing to turbulence produced at the sharp angle. The later Magill modified unions illustrated are much more satisfactory for oral intubation if suction is not needed (a similar type with provision for suction is available) as they provide a smooth gas flow with a wide bore inlet. They are large enough to handle easily and, owing to the ridges, endotracheal tubes do not readily slip off. For nasal intubation, however, they do not lie easily along the nose and form an unnecessary lump, which if pressed upon through the towels tends to deform the nose. I have accordingly had a set of these unions made, which have a curve similar to the original small Magill nasal unions. These have an approximate angle of 60° between the inlet and

"Magill Modified Union" New Nasal Unions

FIG. 1

outlet. In consequence they and the rubber connector lie smoothly along the nose without deforming the nostril. The unions have proved very satisfactory in use and are pleasant to handle.

Experiment has shown that at a flow rate of 15 litres per minute these unions add no measurable resistance to that of the corresponding size of endotracheal tube. Comparative tests with Rowbotham and Cobb Unions show that these produce 100–150 per cent increase in the resistance of an endotracheal tube, measured by water manometer.

ACKNOWLEDGMENT

Thanks are due to Mr. Reed of Medical & Industrial Equipment Ltd., 152-154, Oxford Road, Manchester, for his help in producing these unions.

BOOK REVIEW

La Douleur et Les Douleurs. Published under the direction of Professor Th. Alajouanine by Masson et Cie. Price 2400 francs.

This paper backed volume consists of twenty-three essays on the subject of "Pain" by Frenchmen all of whom are distinguished by their interest in and their contributions to the above subject. It is in reality a little library in itself with a very extensive bibliography. It is bound to be of interest to every doctor, and of very special interest to some; and to none more than to the anaesthetist.

The first paper, by Professor Leriche, recognized as a great authority on the subject of pain, poses the question "What is pain?" and his answer, "Hélas, nous ne le savons pas," is either discouraging or exciting according to the way you take it. After such a beginning it is not surprising to find that opposing views are in the ascendant, unanimity nonexistent. Here are set out the rival theories of Head and Mackenzie on the one hand and those of Leriche and Morley on the other; Von Frey insisting on the specificity of the pain fibres and Goldscheider regarding pain as only the intensification of any peripheral stimulus. There is much of interest in each one of the papers but for the busy anaesthetist the longest, that on "Les douleurs viscérales," is likely to absorb most attention. Here the reader will find at the end of the chapter a table showing a list of the abdominal organs and the spinal roots by which their pain-conveying fibres attain the central nervous system and the paths by which these fibres have travelled. Originally the autonomic system was supposed to contain only motor and secretory fibres. This contention can no longer be held. The distinction between fibres belonging to the c.n.s. and those of the autonomic n.s. rests on the position of their cell stations; fibres of the former have their cell stations in the cerebrospinal axis, the latter have theirs in the ganglia. Section and degeneration experiments show that fibres coming from the wall of the bowel have their cell stations in the posterior root ganglion. Clearly then they belong to the somatic system and not the autonomic. It is true that they run in the sympathetic pathways but "Les fibres sensitives viscérales n'appartiennent pas au système sympathique; elles ne font qu'en emprunter les voies pour rejoindre les racines postérieures." So somatic fibres carry the nerve impulses that lead to pain from the viscus affected (visceral pain proper), from the neighbouring wall (parietal pain), and from the distant sensory area (referred or projected pain). Professor F. Lhermitte has no doubt about this latter, which Mackenzie called the viscerosensory reflex, but he does not accept Mackenzie's explanation. Instead he suggests that the phenomenon is better explained by the three processes of facilitation, convergence and summation. The difference between a somatic and sympathetic nerve supply in no way accounts for the difficulty of localizing the origin of the pain from the deep tissues of the body; rather is the localization of pain a function of the density of the nerve terminations transmitting the pain.

There is a short chapter on morphia that will have a special interest for anaesthetists, but indeed there is much to be learnt from every chapter. Perhaps two or three are less absorbing and somewhat difficult to read, and it is just possible that the tired reader may find that he has been allowing his attention to wander.

E. Falkner Hill

ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

JOHN SNOW, M.D.
Licentiate of the Royal College of Physicians

(*Continued from page* 192)

The word asphyxia has become so closely connected by physiologists with death by privation of air, where the symptoms and appearances are the reverse of those in Chevalier's case, that it is necessary to discard his name of the disease which he describes, although it is etymologically correct. His cases come under the definition of what is now universally called syncope, and what I have called anæmic to distinguish it from cardiac syncope.

Chevalier speaks of a want of power in the vessels to propel the blood, and as it is not now believed that the vessels take any active share in the propulsion of the blood, this may be the reason why the views of this author have received less attention than they deserve; but it very obvious that a want of tone in the vessels, or any great diminution of that power which enables them to support and compress the blood, is an adequate cause why the blood should be unable to reach the right side of the heart. In the case of varicose veins, previously mentioned, it was physically apparent that the cause of the syncope lay in the vessels. Disease of the arteries is well known to be usually associated with degeneration of the heart; the veins are also large and distensible in old people, who furnish the greater number of those who are liable to anæmic syncope; but the pathology of the veins, as regards both their functions and structure, is not yet sufficiently known.

Persons with disease of the heart, who die suddenly in a fit of anger, probably die always with the heart distended; that is, of cardiac syncope. Dr. Joseph Ridge, however, in his able and interesting remarks on the disease and death of John Hunter,* states his belief that that celebrated man, who had been long subject to attacks of angina pectoris, died at last of syncope, with an empty heart. He died, as is well known, during a fit of anger, and the coronary arteries were found ossified. It is not said that the heart was empty, but that it was small, and that there were no coagula in any of its cavities. It is probable that there was not much blood in its cavities at the time of the *post mortem* examination, but the body of Hunter was conveyed in a sedan-chair, from St. George's Hospital, to Leicester Square, a little more than an hour after his death, so that the fluid blood would gravitate downwards. It is related that the stomach and intestines were unusually loaded with blood, and that those parts which were in a depending position, as in the bottom of the pelvis and upon the loins, were congested in a greater degree than the others;

* Oration before the Hunterian Society. Pamphlet, 1855.

and that "this evidently arose from the fluid state of the blood."

In syncope from muscular exertion, the cavities of the heart are distended, and its walls have occasionally been ruptured, both from violent exercise and fits of anger.

Fear probably occasions each kind of syncope in different cases. In some cases, the right cavities of the heart become distended owing to impeded respiration, and possibly to a diminution of power in the heart itself. More frequently, the syncope appears to be of the ordinary or anæmic kind, the effect of the mental condition acting first on the more distant parts of the circulation. The pallor caused by fright is proverbial.

Pain is also capable of causing both kinds of syncope. I have alluded to cases (Page 46, Jan. 1955) in which the patients strained and held their breath till the pulse became intermittent, and the action of the heart was temporarily suspended by the arrested breathing; on the other hand, patients often become pale, if they are undergoing any slight operation when seated, and syncope of the anæmic kind occurs, without any previous disturbance of the respiration, but passes off as soon as they are placed in the horizontal posture. I have seen an apparently strong man faint in this manner, during the removal of a tumour from the back not larger than a nut, and where only a few drops of blood were lost. Chloroform was not employed.

SUPPOSED CAUSES OF DEATH FROM CHLOROFORM

Many writers have supposed that the deaths from chloroform have arisen from some peculiarity in the patient; and when any notable change of structure has been met with after death in any of the vital organs, this has been thought to afford a sufficient explanation of the event; whilst in the cases in which the organs were in a healthy state, surprise has been expressed at the occurrence. In looking over the account of the cases in which the inhalation of chloroform has been fatal, there is reason to conclude, however, that the subjects of them were, as regards health and strength, quite equal to the average of the multitude who have inhaled this agent without ill effects. In fifteen out of the fifty cases above related, there was no examination of the body after death. In one of these fifteen cases, the patient was in a state of debility, and had hectic fever, apparently from the disease of the ankle-joint, for he had no cough; in another of these cases, the patient was reduced to a state of great debility from cancerous disease of the uterus. In fourteen out of the thirty-five cases, in which an examination of the dead body took place, all the chief organs were found to be healthy, if we except the local congestions of blood connected with the mode of dying, and a flabby state of the heart in a few of the cases, which probably depended on its being full of blood at the time of death, or its not being in a state of post mortem rigidity, at the time it was examined.

In one case, No. 25, the only morbid appearances were adhesions of the pleura of small extent; and in No. 47, the only disease was fatty liver. In Case 17, there were signs of chronic disease of the membranes of the brain; and in two cases, Nos. 16 and 22, there was emphysema of the lungs. In the remaining sixteen cases,

there was some alteration of the heart, accompanied in a few instances by disease of other organs. In Cases 23 and 32, there was fat on the surface of the heart, but the structure was not degenerated. In Case 43, the right ventricle was thinned, but not fatty. In Case 44, there were slight deposits on the mitral valve, the heart being otherwise healthy. In Case 50, there were deposits of lymph on the mitral valve and also on the surface of the heart, which was somewhat enlarged. In Case 8, the heart is merely stated to be large; and in Case 27, hypertrophied. In Case 3, the heart was enlarged, pale, and soft, and the lungs were tuberculous. In Case 15 there was said to be some amount of disease of the aortic valves, and some amount of fatty degeneration of the heart. In Case 37, incipient fatty degeneration was present and in Case 40, that of a youth of eighteen, the heart was slightly enlarged, with some amount of fatty degeneration. In Case 46, the right ventricle was thinned and slightly fatty. There remain three Cases, Nos. 30, 33, and 42, in which the fatty degeneration was more decided; and one case, No. 41, in which it is spoken of as being present in an extreme degree. This was in a man, aged sixty-five, the oldest person included amongst those who died from chloroform.

When we consider how common is fatty degeneration of the heart, especially amongst old persons and those for a long time confined to bed, it is very probable that this affection has been proportionately as frequent, amongst the patients who have inhaled chloroform without ill effects, as in the fatal cases of its inhalation.

There are nine of the fatal cases in which the age of the patient is not stated.

In the other forty-one cases, the ages, when grouped in decennial periods, are shown in the following table, the last column of which shows the proportion which the deaths bear at each period to the number living at that period, out of a thousand persons of all ages in England and Wales.

Under 5 years	.	0	. .	0
5 and under 15	. .	3	. .	$\frac{1}{78}$
15 „ 25	. .	11	. .	$\frac{1}{18}$
25 „ 35	. .	10	. .	$\frac{1}{13}$
35 „ 45	. .	11	. .	$\frac{1}{10}$
45 „ 55	. .	3	. .	$\frac{1}{27}$
55 „ 65	. .	2	. .	$\frac{1}{26}$
65 and upwards	. .	1	. .	$\frac{1}{44}$

The nine persons whose ages are not given were all adults; one is spoken of as a young man, and another as a young woman, and the rest are mentioned in such a manner that it is certain they were not old people. It follows, therefore, that so far as is known, there has been a complete immunity from death by chloroform at both extremes of life. I have already given my reasons for rejecting Dr. Aschendorf's case of an infant, and also the case of a gentleman, aged seventy-three, who died whilst inhaling chloroform. The youngest patient who died from chloroform was seven or eight years of age, and the oldest sixty-five, being the only death above sixty. The above table of the ages shows that the number of deaths, in proportion to the number living, increased rapidly after the age of twenty-five, and decreased rapidly after the age of forty-five.

(To be continued)

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